

US008926540B2

(12) **United States Patent**
Lo et al.

(10) **Patent No.:** **US 8,926,540 B2**
(45) **Date of Patent:** **Jan. 6, 2015**

(54) **HEMODIALYSIS SYSTEM WITH SEPARATE DIALYSATE CASSETTE**

(75) Inventors: **Ying-Cheng Lo**, Green Oaks, IL (US);
Robert W. Childers, Trinity, FL (US);
Thomas D. Kelly, Highland Park, IL (US);
Justin Rohde, Des Plaines, IL (US)

(73) Assignees: **Baxter Healthcare Inc.**, Deerfield, IL (US);
Baxter Healthcare S.A., Glattpark (Opfikon) (CH)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 645 days.

(21) Appl. No.: **13/213,812**

(22) Filed: **Aug. 19, 2011**

(65) **Prior Publication Data**

US 2011/0297598 A1 Dec. 8, 2011

Related U.S. Application Data

(63) Continuation of application No. 11/530,842, filed on Sep. 11, 2006, now Pat. No. 8,038,639, which is a continuation-in-part of application No. 10/982,170, filed on Nov. 4, 2004, now Pat. No. 8,029,454.

(60) Provisional application No. 60/517,730, filed on Nov. 5, 2003.

(51) **Int. Cl.**

A61M 1/38 (2006.01)
A61M 1/14 (2006.01)
A61M 1/16 (2006.01)
A61M 1/28 (2006.01)
A61M 1/34 (2006.01)

(52) **U.S. Cl.**

CPC **A61M 1/16** (2013.01); **A61M 1/1635** (2014.02); **A61M 1/28** (2013.01); **A61M 1/34** (2013.01); **A61M 2205/127** (2013.01)
USPC **604/5.01**; **604/6.13**; **604/4.01**

(58) **Field of Classification Search**

CPC A61M 1/16; A61M 1/28; A61M 1/34; A61M 2205/127

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,774,762 A 11/1973 Lichtenstein
3,912,455 A 10/1975 Lichtenstein

(Continued)

FOREIGN PATENT DOCUMENTS

DE 20 02 033 8/1970
DE 29 01 628 7/1980

(Continued)

OTHER PUBLICATIONS

U.S. Appl. No. 13/213,350, filed Aug. 19, 2011, Kelly et al.

(Continued)

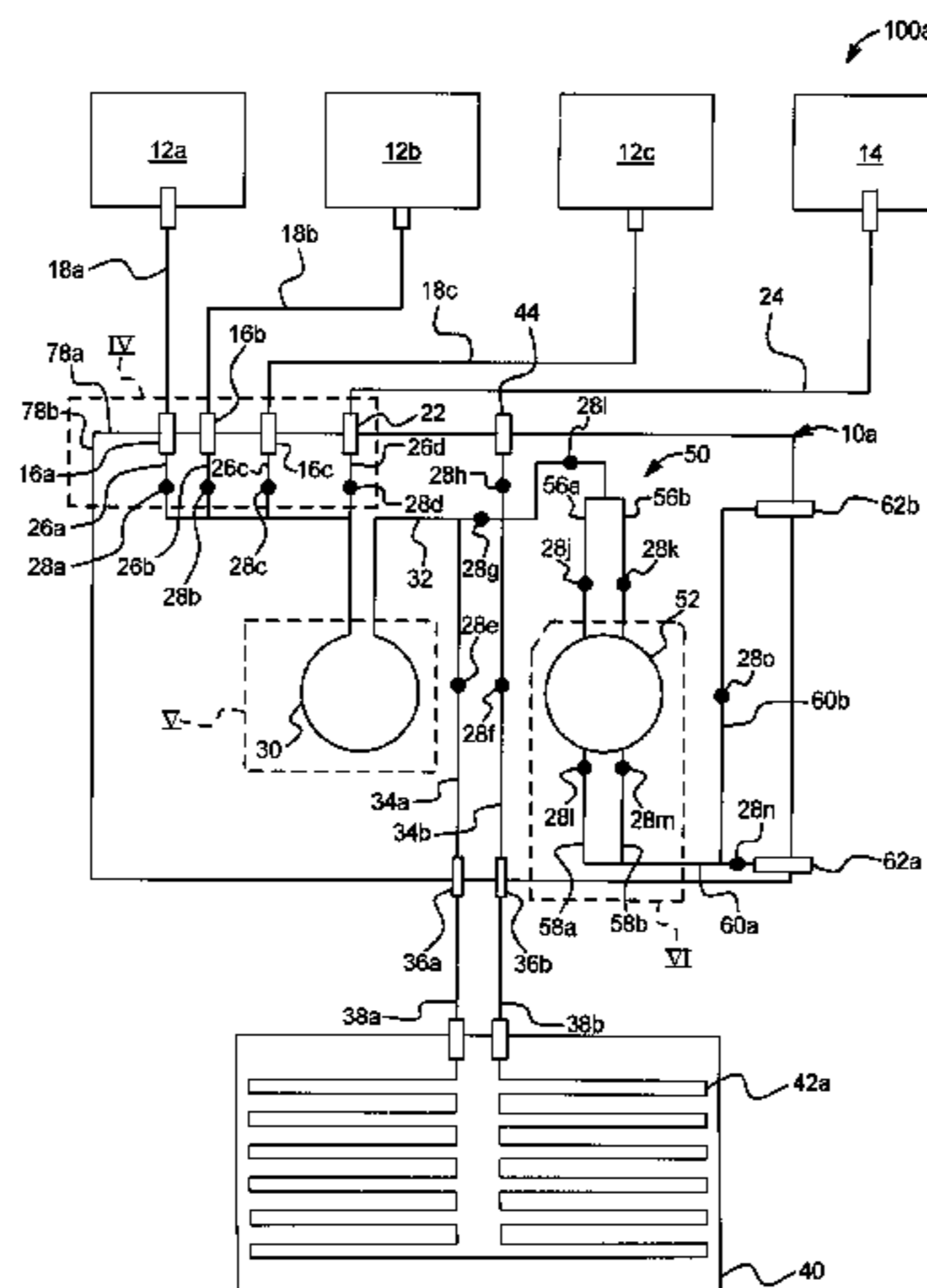
Primary Examiner — Susan Su

(74) *Attorney, Agent, or Firm* — K&L Gates LLP

(57) **ABSTRACT**

A hemodialysis system includes (i) a dialyzer; (ii) a blood pump; (iii) a blood cassette operatively connected to the dialyzer and the blood pump; (iv) a dialysate heater; (v) first and second peristaltic dialysate pumps; and (vi) a dialysate cassette separate from the blood cassette, the dialysate cassette including an organizer configured to support a drain tube, a to-dialyzer tube and a from-dialyzer tube, the cassette further including a first pumping tube, a second pumping tube and an inline fluid heating pathway, the cassette when mounted for operation orienting (a) the first pumping tube for operation with the first peristaltic dialysate pump, (b) the second pumping tube for operation with the second peristaltic dialysate pump and (c) the fluid heating pathway for operation with the dialysate heater.

20 Claims, 35 Drawing Sheets



(56)

References Cited

U.S. PATENT DOCUMENTS

3,946,731 A 3/1976 Lichtenstein
 4,161,264 A 7/1979 Malmgren et al.
 4,190,536 A 2/1980 Grimsrud
 4,209,391 A 6/1980 Landau et al.
 4,244,816 A 1/1981 Vogler et al.
 4,366,061 A 12/1982 Papanek et al.
 4,386,634 A 6/1983 Stasz et al.
 4,464,172 A 8/1984 Lichtenstein
 4,468,329 A 8/1984 Shaldon et al.
 4,477,342 A 10/1984 Allan et al.
 4,479,760 A 10/1984 Bilstad et al.
 4,650,458 A 3/1987 Dahlberg et al.
 4,676,905 A 6/1987 Nagao et al.
 4,702,829 A 10/1987 Polaschegg et al.
 4,708,802 A 11/1987 Rath et al.
 4,767,399 A 8/1988 Bollish
 4,770,769 A 9/1988 Schael
 4,838,865 A 6/1989 Flank et al.
 5,114,580 A 5/1992 Ahmad et al.
 5,173,125 A 12/1992 Felding
 5,221,267 A 6/1993 Folden
 5,288,463 A 2/1994 Chemelli
 5,318,556 A 6/1994 Avallone et al.
 5,324,422 A 6/1994 Colleran et al.
 D350,822 S 9/1994 Lanigan
 D350,823 S 9/1994 Lanigan
 5,350,357 A 9/1994 Kamen et al.
 D357,312 S 4/1995 Riquier et al.
 5,421,823 A 6/1995 Kamen et al.
 5,441,636 A 8/1995 Chevallet et al.
 5,470,483 A 11/1995 Bene et al.
 5,522,998 A 6/1996 Polaschegg
 5,542,919 A 8/1996 Simon et al.
 5,570,026 A 10/1996 Buffaloe, IV et al.
 5,614,677 A 3/1997 Wansiedler et al.
 5,702,597 A 12/1997 Chevallet et al.
 5,730,712 A 3/1998 Falkvall et al.
 5,836,908 A 11/1998 Beden et al.
 5,846,419 A 12/1998 Nederlof
 5,863,421 A 1/1999 Peter, Jr. et al.
 5,871,694 A 2/1999 Beden et al.
 5,919,369 A 7/1999 Ash
 5,925,011 A 7/1999 Faict et al.
 5,928,744 A 7/1999 Heilmann et al.
 5,932,799 A 8/1999 Moles
 5,989,423 A 11/1999 Kamen et al.
 6,004,311 A 12/1999 Heilmann et al.
 6,042,784 A 3/2000 Wamsiedler et al.
 6,110,384 A 8/2000 Goux et al.
 6,126,831 A 10/2000 Goldau et al.
 6,139,748 A 10/2000 Ericson et al.
 6,210,361 B1 4/2001 Kamen et al.
 6,254,567 B1 7/2001 Treu et al.
 6,260,715 B1 7/2001 Simard et al.
 6,280,632 B1 8/2001 Polaschegg
 6,287,516 B1 9/2001 Matson et al.
 6,322,551 B1 11/2001 Brugger
 6,364,857 B1 4/2002 Gray et al.
 6,382,923 B1 5/2002 Gray
 6,454,736 B1 9/2002 Ludt et al.
 6,484,383 B1 11/2002 Herklotz
 6,491,656 B1 12/2002 Morris
 6,495,366 B1 12/2002 Briggs
 6,531,061 B1 3/2003 Cholewa
 6,554,789 B1 4/2003 Brugger et al.
 6,572,576 B2 6/2003 Brugger et al.
 6,572,641 B2 6/2003 Brugger et al.
 6,579,253 B1 6/2003 Burbank et al.
 6,582,385 B2 6/2003 Burbank et al.
 6,589,482 B1 7/2003 Burbank et al.
 6,620,120 B2 9/2003 Landry et al.
 6,638,477 B1 10/2003 Treu et al.
 6,638,478 B1 10/2003 Treu et al.
 6,649,063 B2 11/2003 Brugger et al.
 6,663,359 B2 12/2003 Gray

6,702,561 B2 3/2004 Stillig et al.
 6,743,201 B1 6/2004 Donig et al.
 6,752,172 B2 6/2004 Lauer
 6,764,460 B2 7/2004 Dolecek et al.
 6,770,049 B2 8/2004 Ludt et al.
 6,821,441 B2 11/2004 Pedrini et al.
 6,830,553 B1 12/2004 Burbank et al.
 6,843,779 B1 1/2005 Andrysiak et al.
 6,852,090 B2 2/2005 Burbank et al.
 7,112,273 B2 9/2006 Weigel et al.
 7,115,107 B2 10/2006 Delnevo et al.
 7,300,413 B2 11/2007 Burbank et al.
 2001/0021817 A1 9/2001 Brugger et al.
 2001/0032818 A1 10/2001 Nikaido et al.
 2001/0037079 A1 11/2001 Burbank et al.
 2001/0045395 A1 11/2001 Kitaevich et al.
 2002/0017489 A1 2/2002 Utterberg
 2002/0041825 A1 4/2002 Scheunert et al.
 2002/0072718 A1 6/2002 Brugger et al.
 2002/0082728 A1 6/2002 Mueller et al.
 2002/0103453 A1 8/2002 Burbank et al.
 2002/0147423 A1 10/2002 Burbank et al.
 2003/0010717 A1 1/2003 Brugger et al.
 2003/0010718 A1 1/2003 Burbank et al.
 2003/0018290 A1 1/2003 Brugger et al.
 2003/0036719 A1 2/2003 Giacomelli et al.
 2003/0047184 A1 3/2003 Lockhart et al.
 2004/0019312 A1 1/2004 Childers et al.
 2004/0019314 A1 1/2004 Delnevo
 2004/0069709 A1 4/2004 Brugger et al.
 2004/0138607 A1 7/2004 Burbank et al.
 2004/0158189 A1 8/2004 Tonelli et al.
 2004/0176724 A1 9/2004 Kamen et al.
 2004/0186416 A1 9/2004 Caleffi
 2004/0238416 A1 12/2004 Burbank et al.
 2004/0243046 A1 12/2004 Brugger et al.
 2004/0243047 A1 12/2004 Brugger et al.
 2004/0243048 A1 12/2004 Brugger et al.
 2004/0243049 A1 12/2004 Brugger et al.
 2004/0243050 A1 12/2004 Treu et al.
 2004/0245161 A1 12/2004 Treu et al.
 2004/0249331 A1 12/2004 Burbank et al.
 2004/0267184 A1 12/2004 Burbank et al.
 2004/0267185 A1 12/2004 Weaver et al.
 2005/0000868 A1 1/2005 Weigel et al.
 2005/0004502 A1 1/2005 O'Mahony et al.
 2005/0010158 A1 1/2005 Brugger et al.
 2005/0011823 A1 1/2005 Delnevo et al.
 2005/0020959 A1 1/2005 Brugger et al.
 2005/0020960 A1 1/2005 Brugger et al.
 2005/9020958 1/2005 Paolini et al.
 2005/0095141 A1 5/2005 Lanigan et al.
 2005/0096583 A1 5/2005 Demers et al.
 2005/0131332 A1 6/2005 Kelly et al.
 2005/0230292 A1 10/2005 Beden et al.
 2006/0084906 A1 4/2006 Burbank et al.
 2007/0129707 A1 6/2007 Blott et al.
 2008/0208103 A1 8/2008 Demers et al.
 2009/0101549 A1 4/2009 Kamen et al.

FOREIGN PATENT DOCUMENTS

DE 31 22 756 6/1982
 DE 33 07 830 6/1984
 DE 40 03 452 8/1991
 DE 42 08 054 10/1992
 DE 41 22 754 1/1993
 DE 198 30 928 C1 5/1999
 DE 198 14 695 A1 10/1999
 DE 198 54 338 6/2000
 DE 100 11 208 C1 9/2001
 DE 101 00 146 A1 7/2002
 EP 0 143 341 6/1985
 EP 0165751 6/1985
 EP 0165751 A2 12/1985
 EP 0 166 920 A1 1/1986
 EP 0 233 848 8/1987
 EP 0 306 241 A2 3/1989
 EP 0 373 455 6/1990

(56)

References Cited

FOREIGN PATENT DOCUMENTS

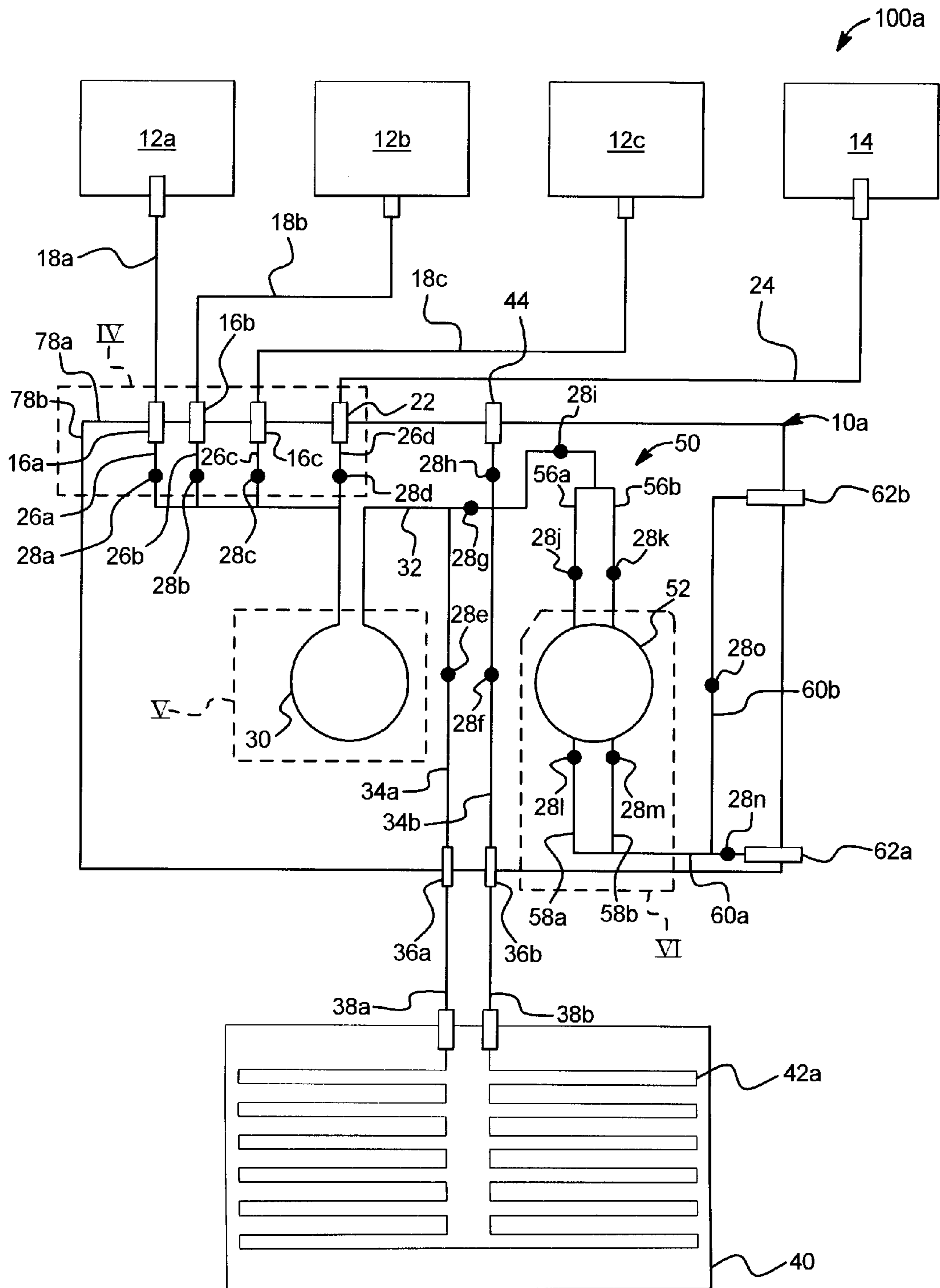
EP	0 222 709	5/1991
EP	0 490 212	6/1992
EP	0 623 357 A1	11/1994
EP	0 722 744	7/1996
EP	0 796 998 A1	9/1997
EP	0 659 091	12/2000
EP	1 097 724	5/2001
EP	1 235 613	8/2009
FR	78 31918	2/1979
FR	2 585 251	1/1987
GB	1 492 387	11/1977
GB	2 014 060	8/1979
GB	2 246 718 A	2/1992
JP	61-008057	1/1986
JP	07-035413	2/1995
JP	11 226121	8/1999
JP	2000-84071	3/2000
JP	217908	8/2000
JP	296318	10/2000
JP	2003518964	6/2003
JP	2004-205146	7/2004
JP	2004-209103	7/2004
JP	2006-500968	1/2006
RU	1001945	3/1983
RU	1821222	6/1993
WO	WO 98/22165	5/1998
WO	WO 98/32477	7/1998
WO	WO 99/42150	8/1999
WO	WO 00/09182	2/2000
WO	WO 00/31967	6/2000
WO	WO 00/57925	10/2000
WO	WO 00/57926	10/2000
WO	WO 00/57927	10/2000
WO	WO 00/64510	11/2000
WO	WO 01/37786	5/2001
WO	WO 01/37894	5/2001
WO	WO 01/37895	5/2001
WO	WO 01/37900	5/2001
WO	WO 01/41831	6/2001
WO	WO 01/41832	6/2001
WO	WO 01/42758	6/2001
WO	WO 01/45769	6/2001
WO	WO 0141833	6/2001
WO	01/47581 A1	7/2001
WO	WO 01/47576	7/2001
WO	WO 02/070042	9/2002
WO	03/011376	2/2003
WO	03/041764	5/2003
WO	2004/082731	9/2004
WO	2005/042065	5/2005
WO	2005/044339	5/2005
WO	2005/044339 A2	5/2005
WO	2005/044340	5/2005
WO	WO 2005/044339	5/2005
WO	WO 2006/105605	10/2006
WO	WO 2007/074425	7/2007
WO	WO 2008/033788	3/2008

OTHER PUBLICATIONS

U.S. Appl. No. 13/213,358, filed Aug. 19, 2011, Kelly et al.

U.S. Appl. No. 13/213,676, filed Aug. 19, 2011, Lo et al.
 U.S. Appl. No. 13/213,692, filed Aug. 19, 2011, Lo et al.
 U.S. Appl. No. 13/213,737, filed Aug. 19, 2011, Childers et al.
 U.S. Appl. No. 13/213,727, filed Aug. 19, 2011, Childers et al.
 U.S. Appl. No. 13/213,707, filed Aug. 19, 2011, Childers et al.
 International Search Report and the Written Opinion for International Application No. PCT/US2008/064086 mailed on Jan. 27, 2009.
 European Office Action received by foreign associate on Sep. 26, 2013 for related European Appln. No. 11075129.4.
 European Office Action received by foreign associate on Sep. 30, 2013 for related European Appln. No. 11075130.2.
 European Office Action received by foreign associate on Sep. 30, 2013 for related European Appln. No. 11185112.7.
 European Office Action received by foreign associate on Sep. 26, 2013 for related European Appln. No. 11185090.5.
 European Search Report for European Application No. 11 07 5124 mailed on Mar. 16, 2012.
 European Search Report for European Application No. 11 07 5125 mailed on Mar. 26, 2012.
 European Search Report for European Application No. 11 07 5126 mailed on Mar. 22, 2012.
 European Search Report for European Application No. 11 07 5127 mailed on Mar. 28, 2012.
 European Search Report for European Application No. 11 07 5128 mailed on Apr. 3, 2012.
 European Search Report for European Application No. 11 07 5129 mailed on Mar. 29, 2012.
 European Office Action issued Aug. 20, 2013 for related European Appln. No. 11075128.6.
 Extended European Search Report for European Application No. 11075130.2 mailed on Mar. 15, 2012.
 Manns et al., The acu-men™: A new device for continuous renal replacement therapy in acute renal failure, *Kidney International*, 1998, pp. 268-74, vol. 54.
 European Search Report for European Application No. EP 11 18 5090 mailed on Dec. 22, 2011.
 European Search Report for European Application No. EP 11 18 5112 mailed on Dec. 20, 2011.
 Japanese Office Action Mailed Dec. 20, 2012 for corresponding Japanese Appln. No. 2010-514907.
 European Office Action dated Feb. 12, 2013 for related European Appln. No. 11075124.5.
 Japanese Office Action Received Sep. 18, 2012 for corresponding Japanese Appln. No. 2009-527618.
 Japanese Office Action mailed Jan. 10, 2014 for related Japanese Appln. No. 2013/000322.
 European Office Action received Mar. 14, 2013 for related European Appln. No. 11075126.0.
 European Search Report issued Mar. 26, 2012, corresponding to European Appln. No. 11075125.2.
 European Office Action issued Jun. 6, 2013 for related European Appln. No. 11075125.2.
 European Office Action issued Apr. 18, 2013 for related European Appln. No. 11075127.8.
 Japanese Office Action mailed Jan. 30, 2014 in corresponding Japanese Patent Application No. 2011-163710.
 European Office Action mailed Aug. 7, 2014 for related European Appln. No. 11075128.6 (5 pages).
 Japanese of Action mailed Jun. 30, 2014 for related Japanese Appln. No. 2013-169818 (10 pages).

FIG. 1



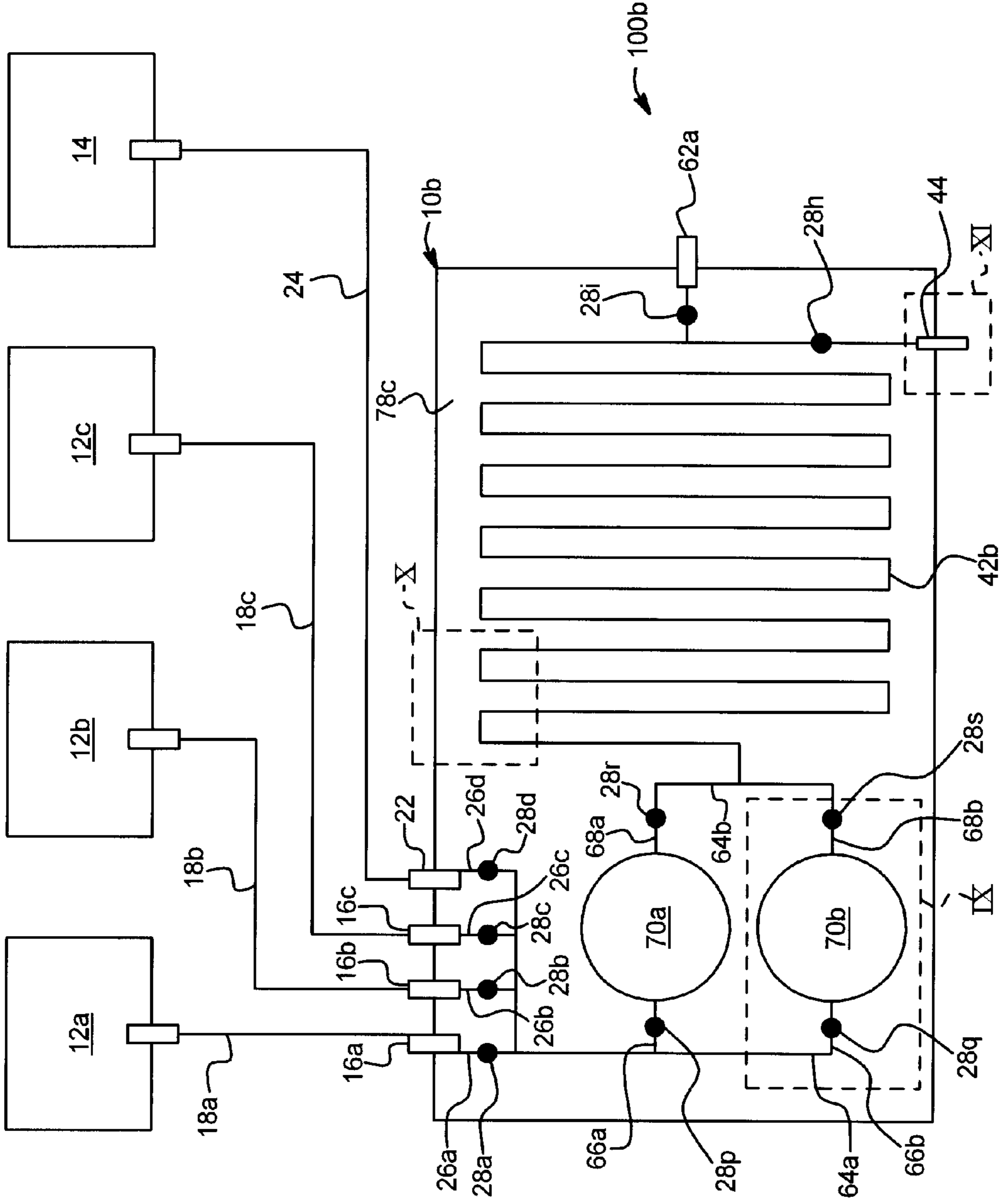


FIG. 2

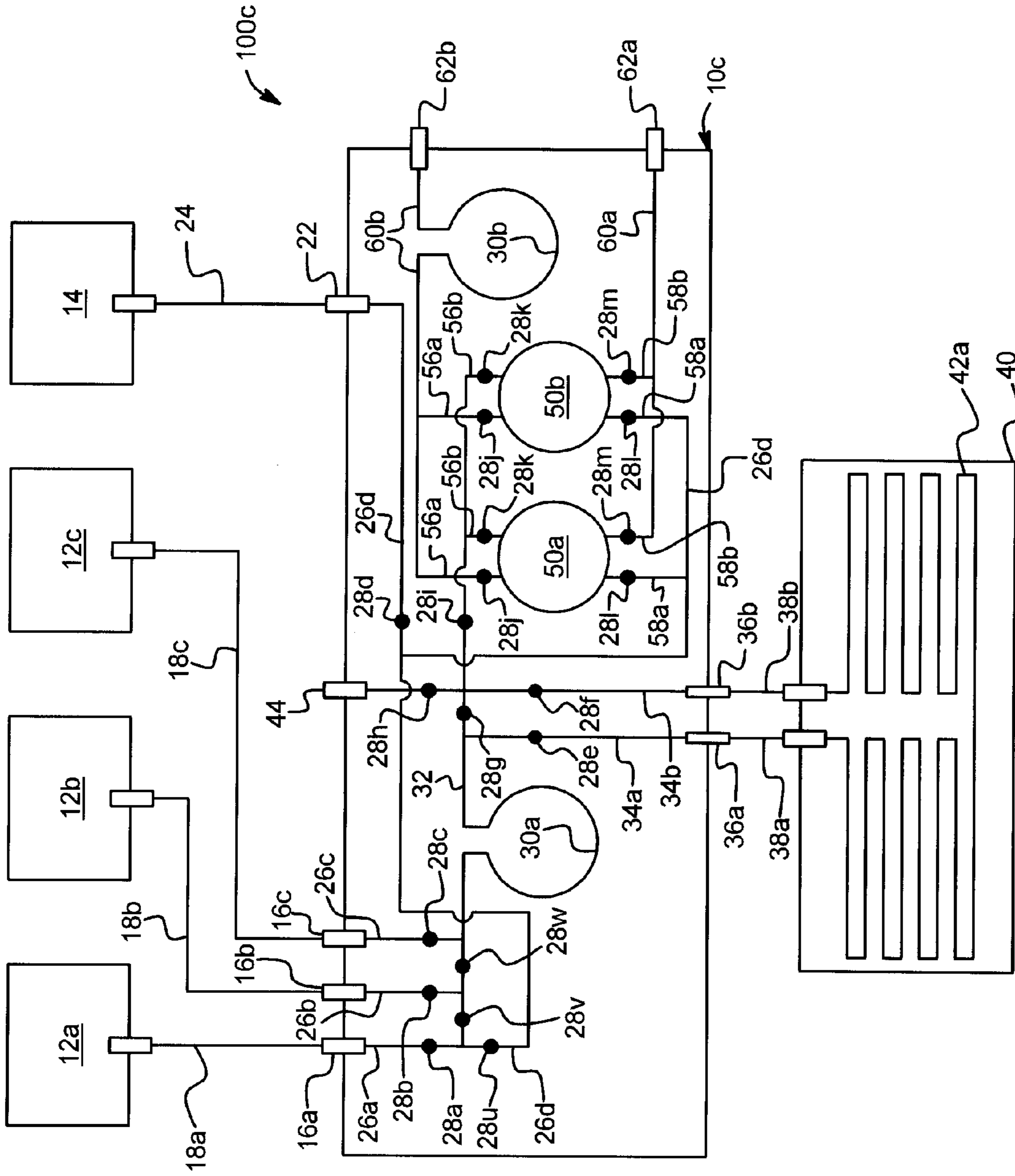
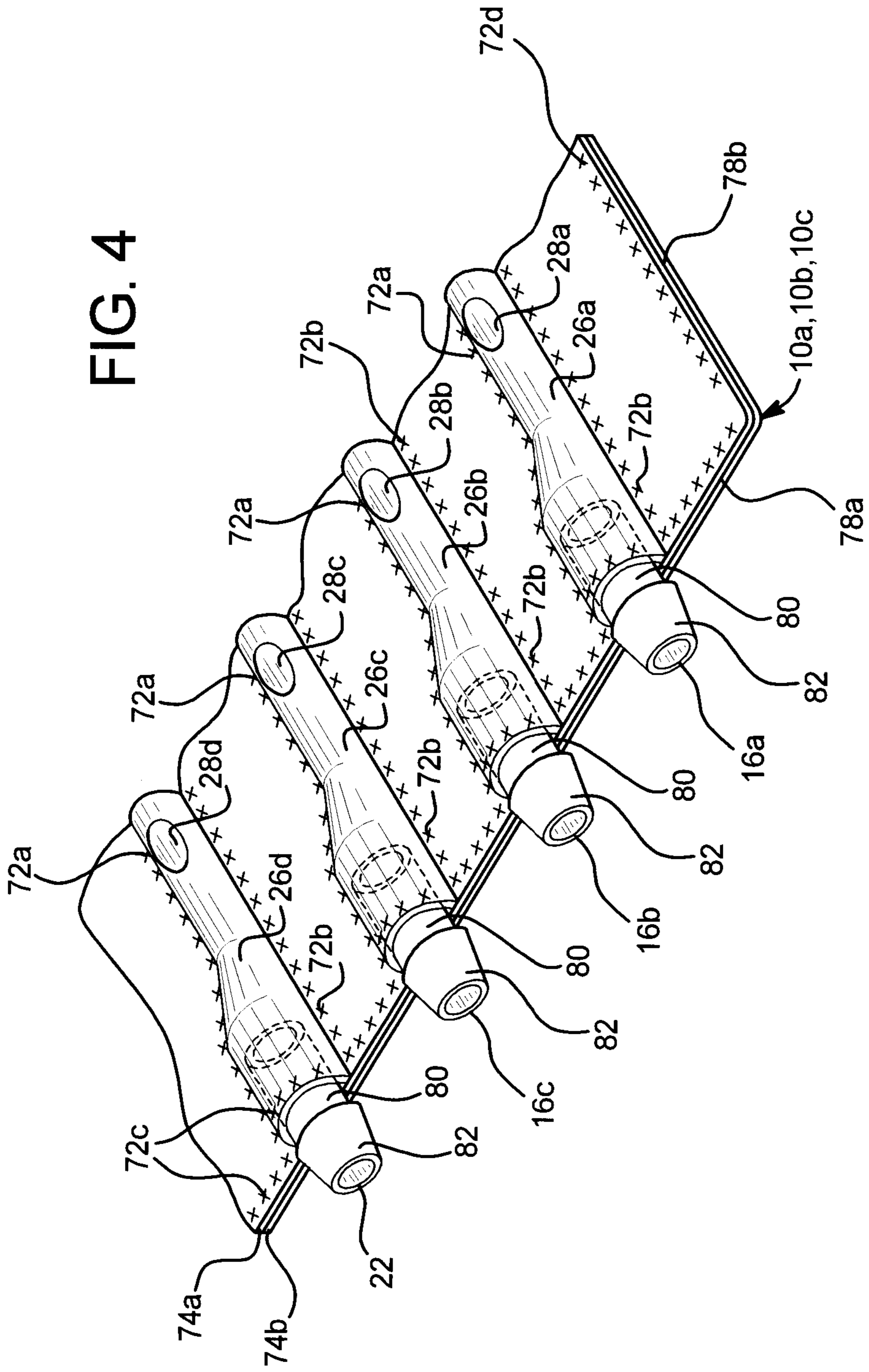


FIG. 3

FIG. 4



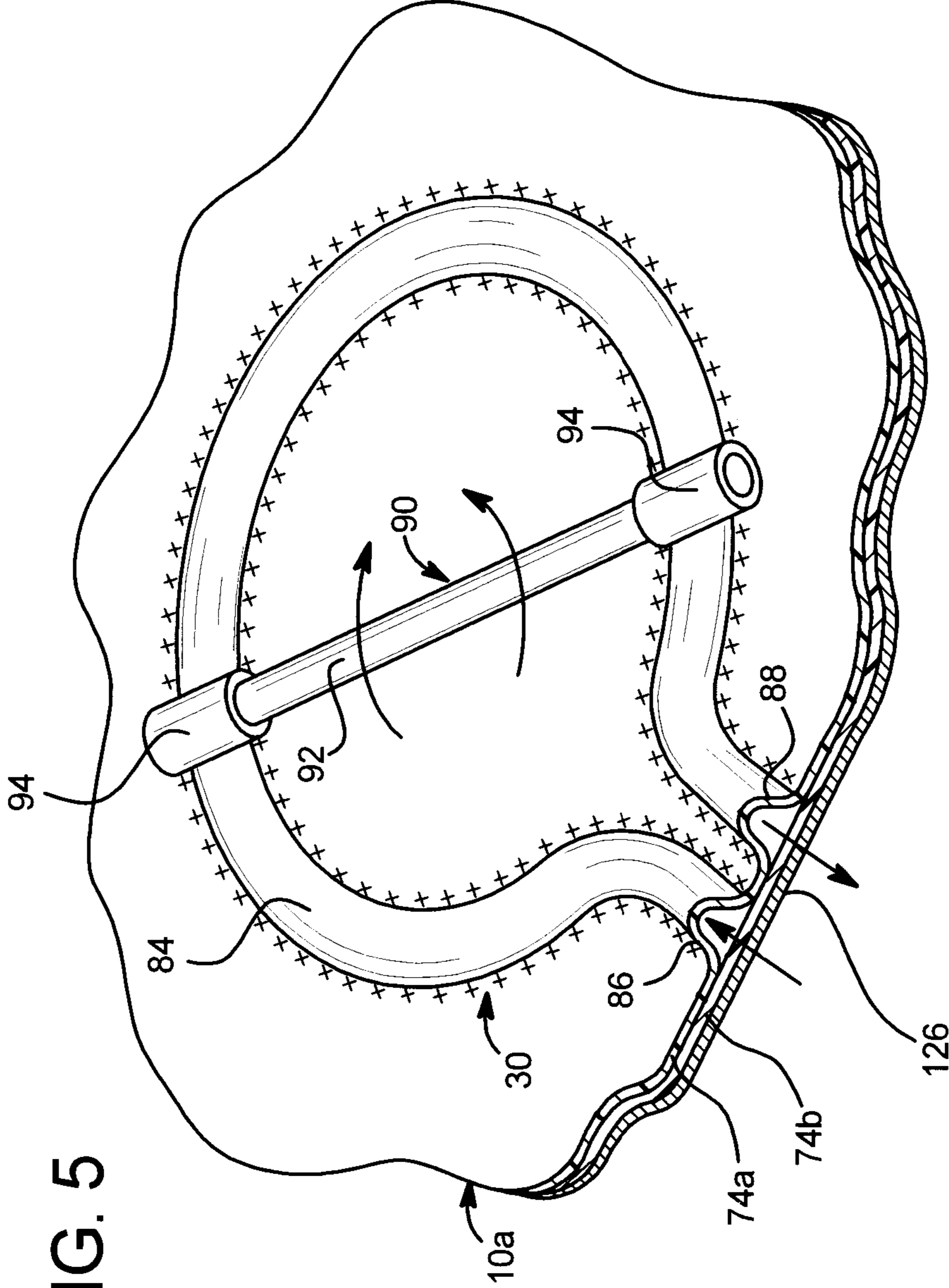


FIG. 5

FIG 6

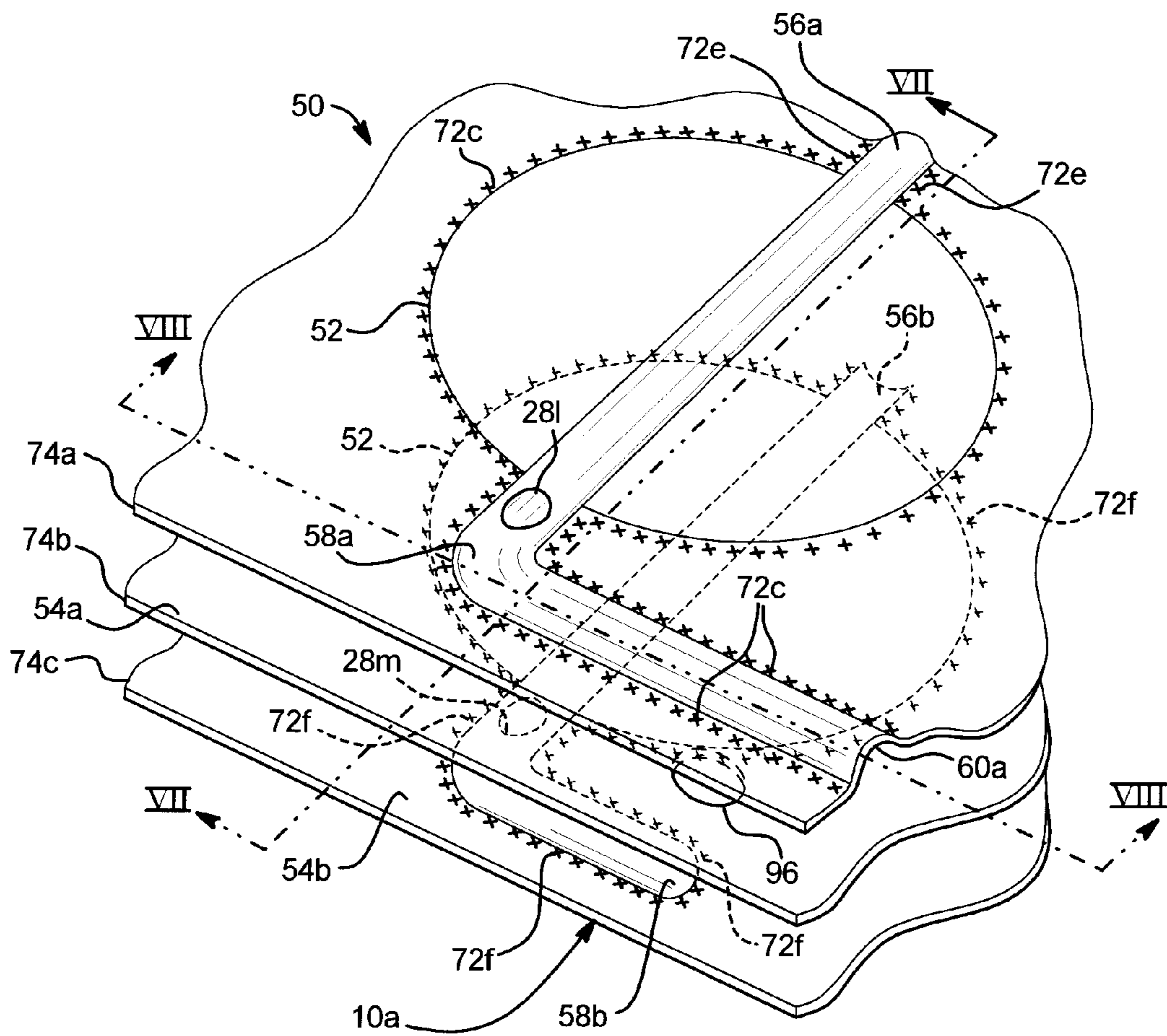


FIG. 7

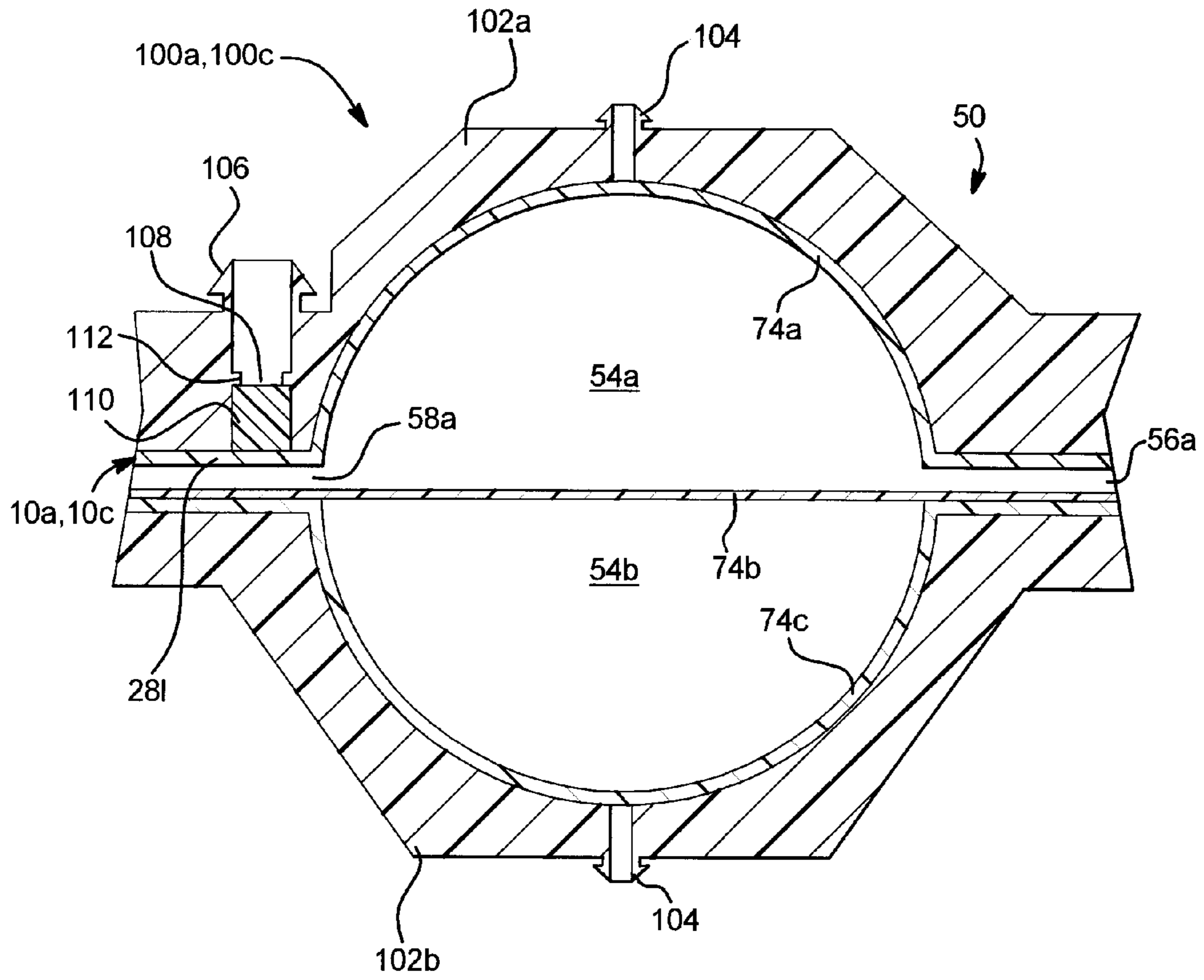
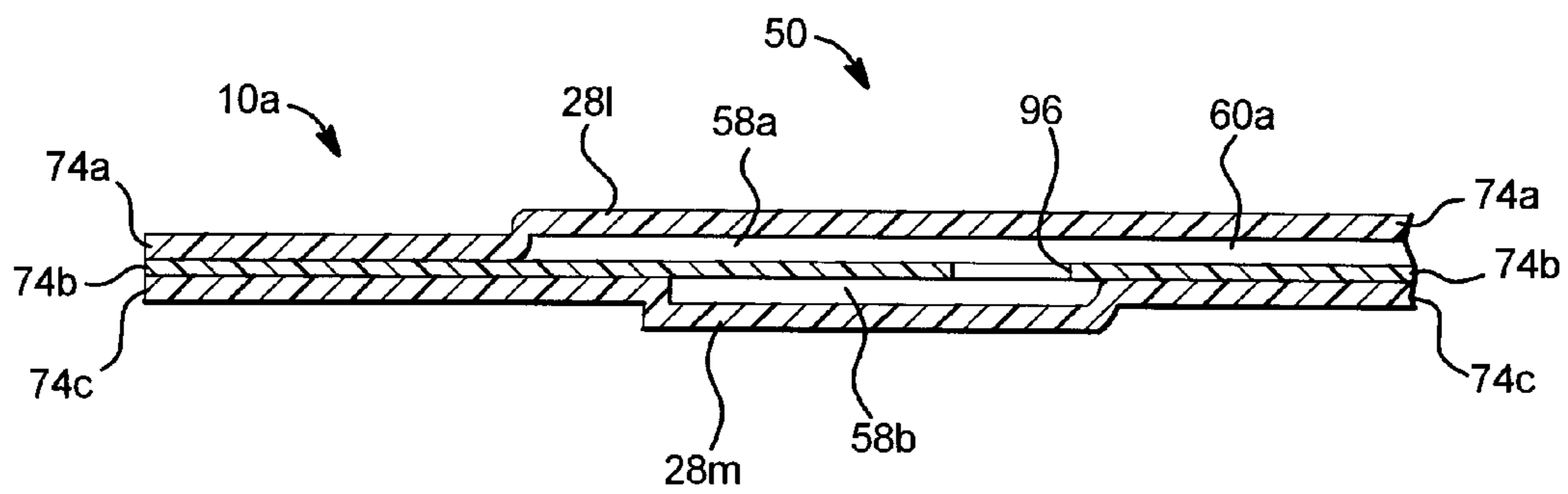
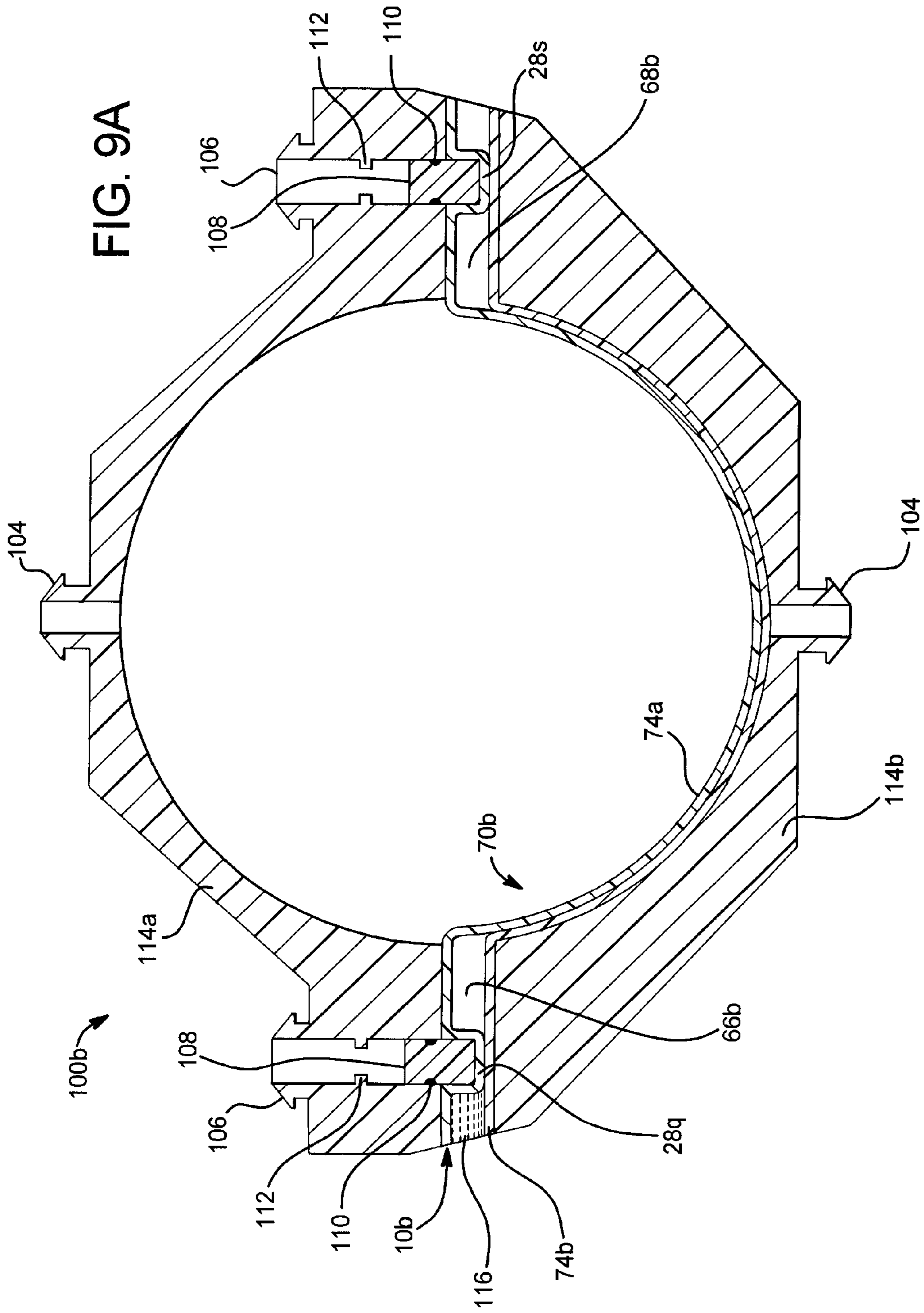
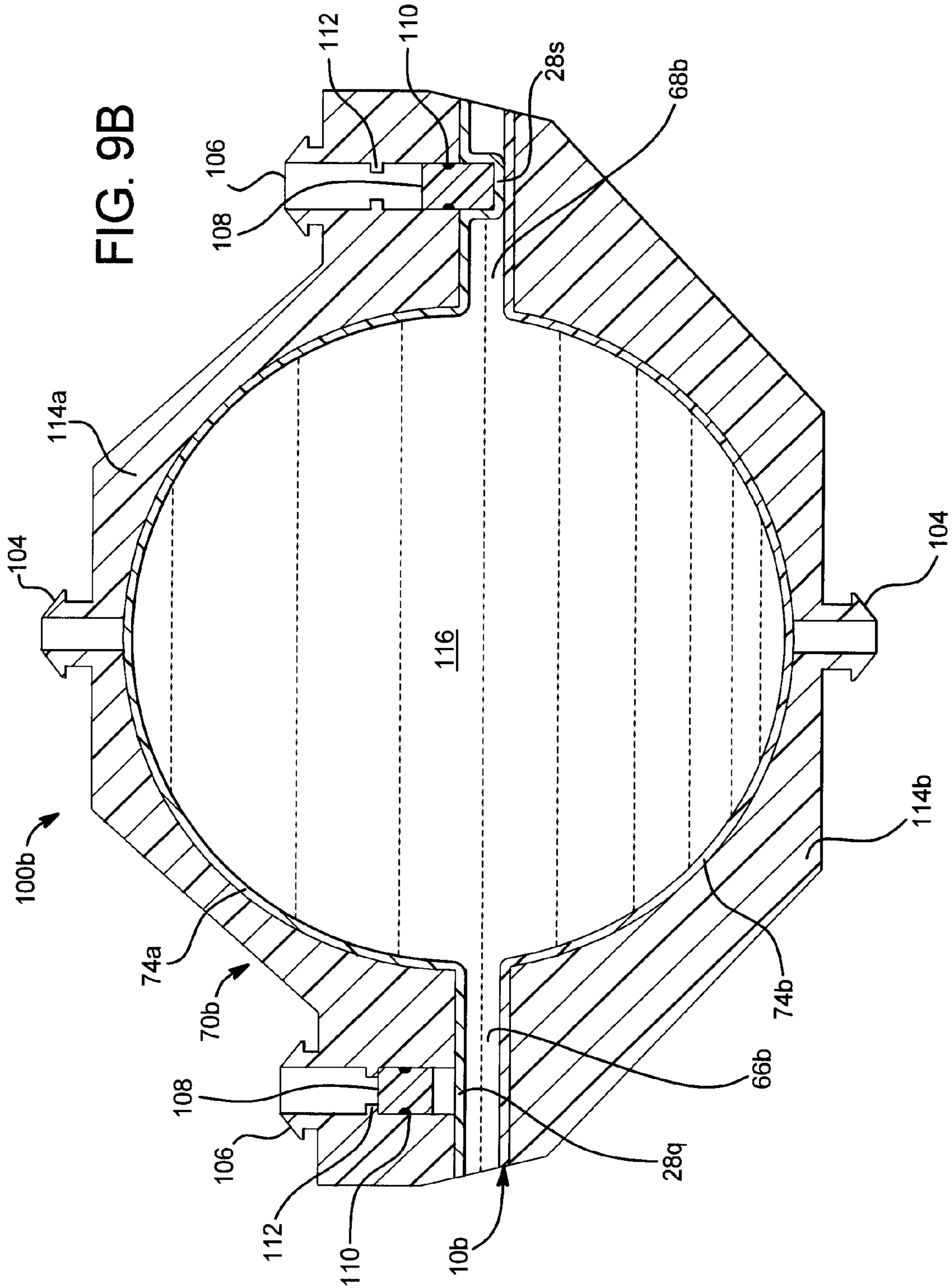


FIG. 8







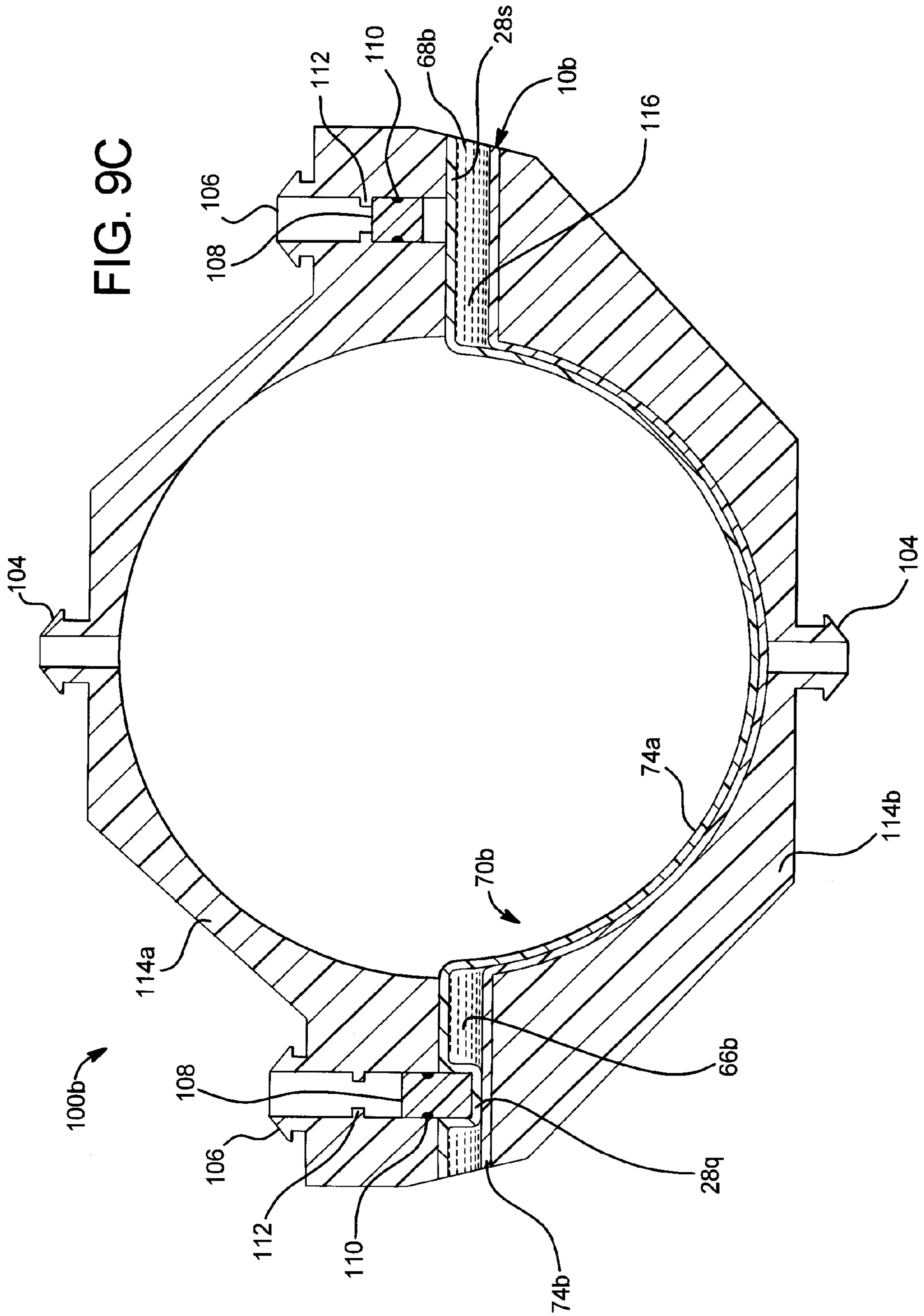


FIG. 10A

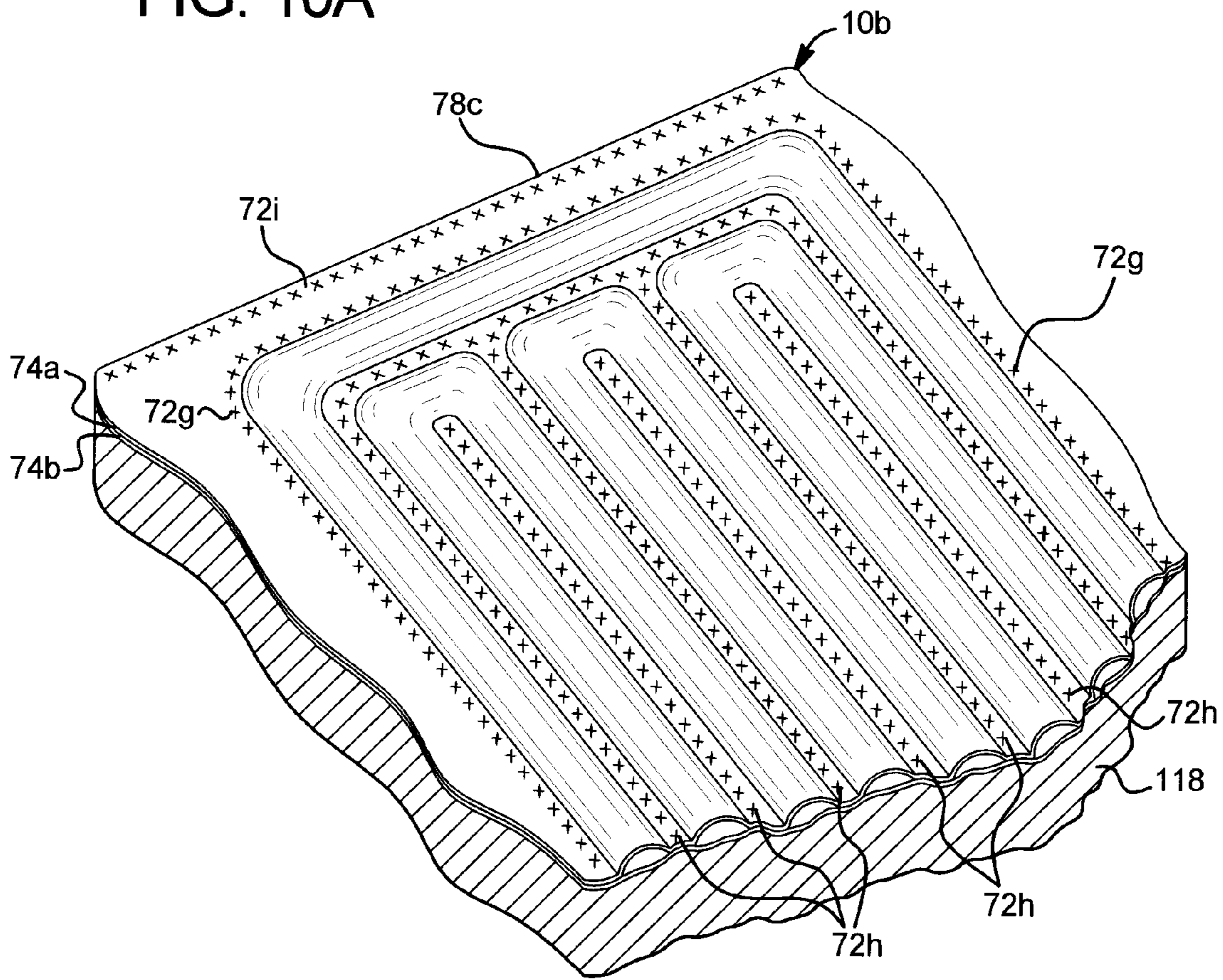


FIG. 10B

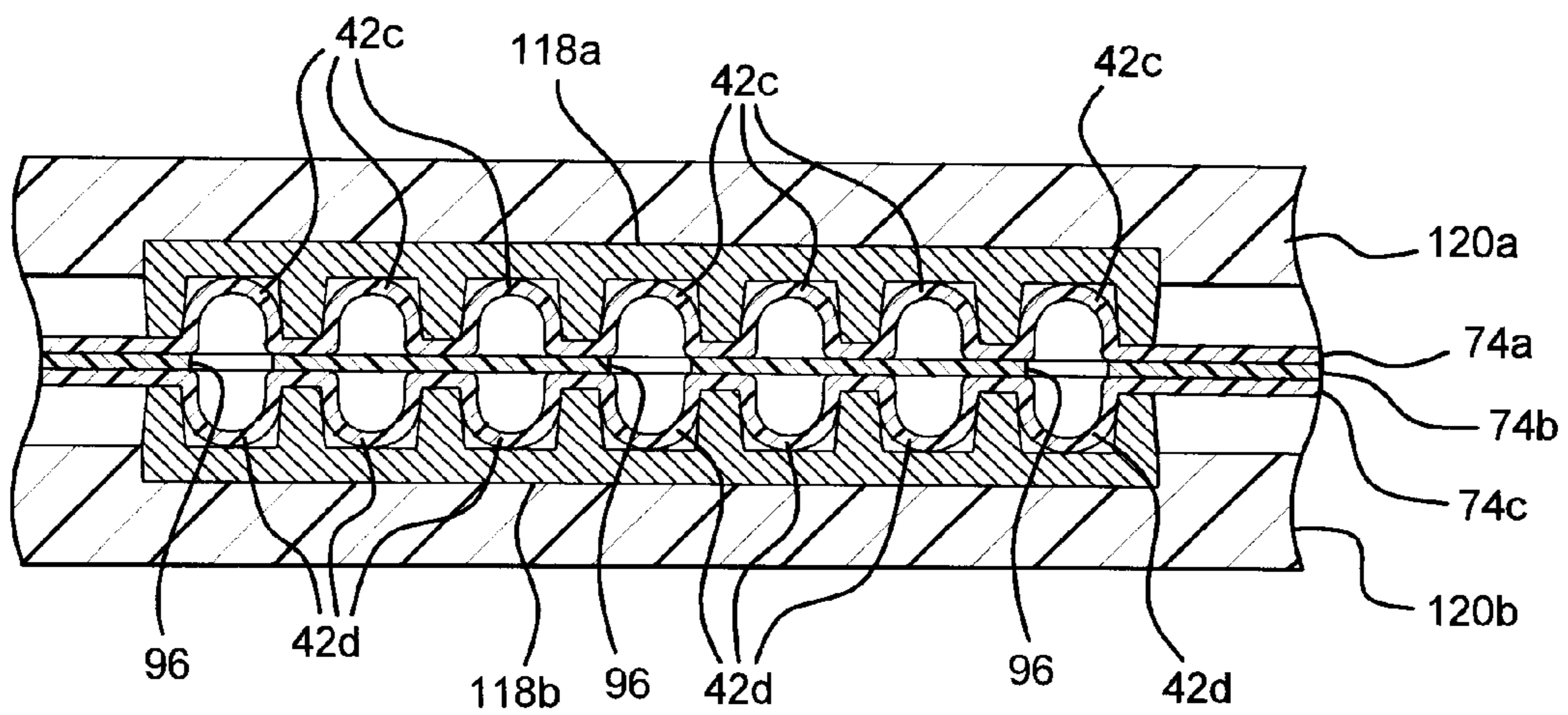


FIG. 11

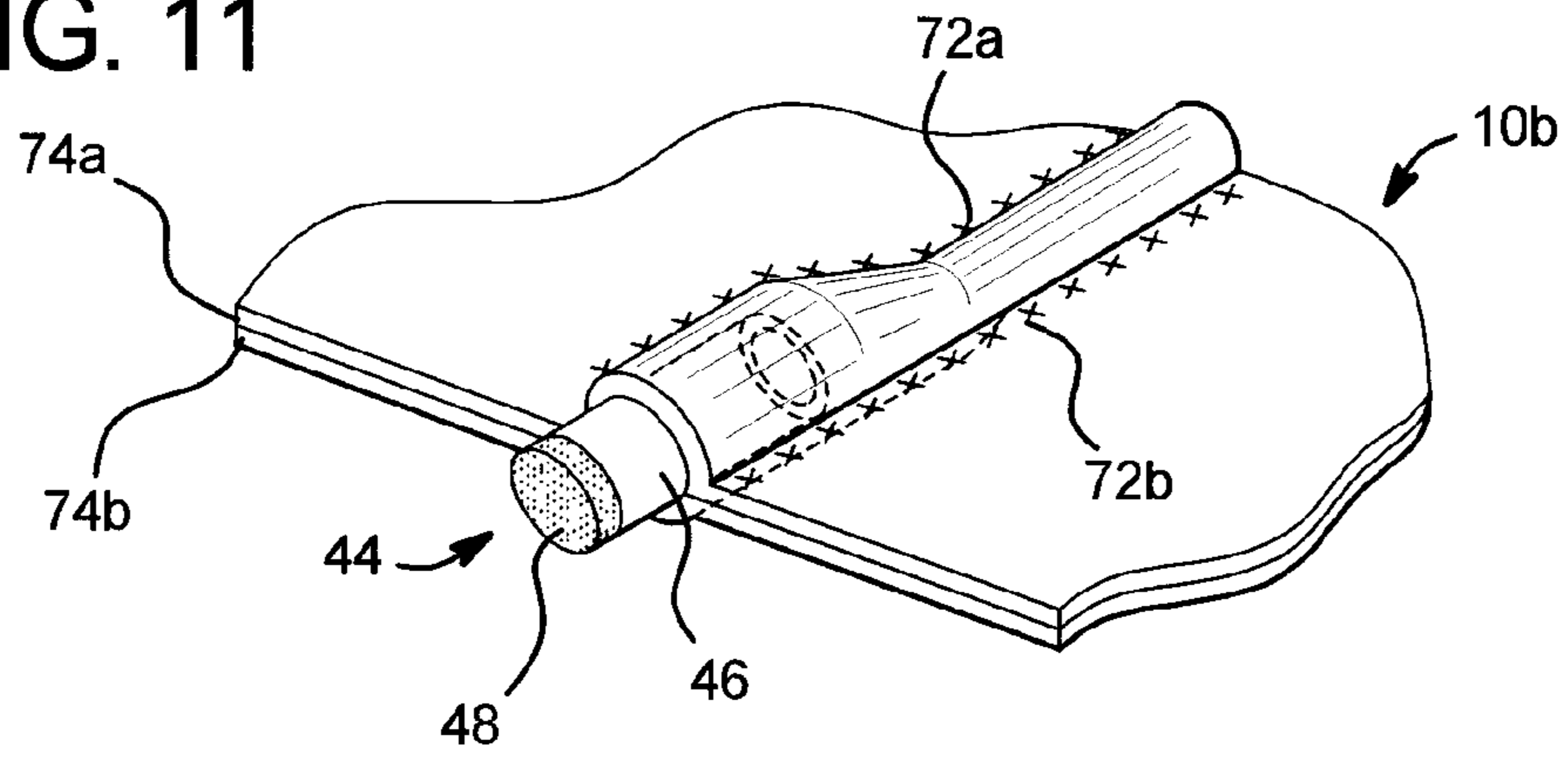


FIG. 12A

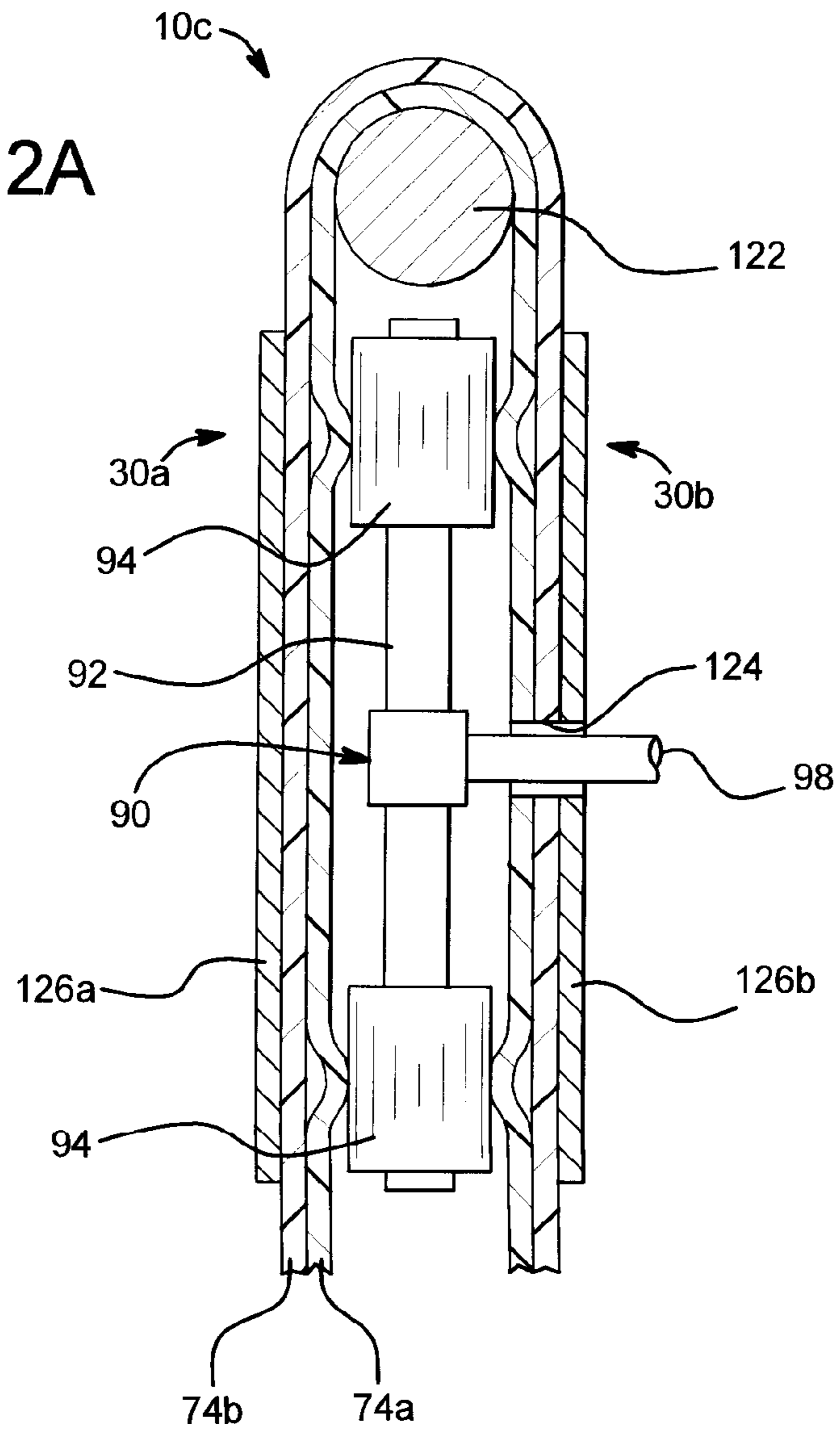


FIG. 12B

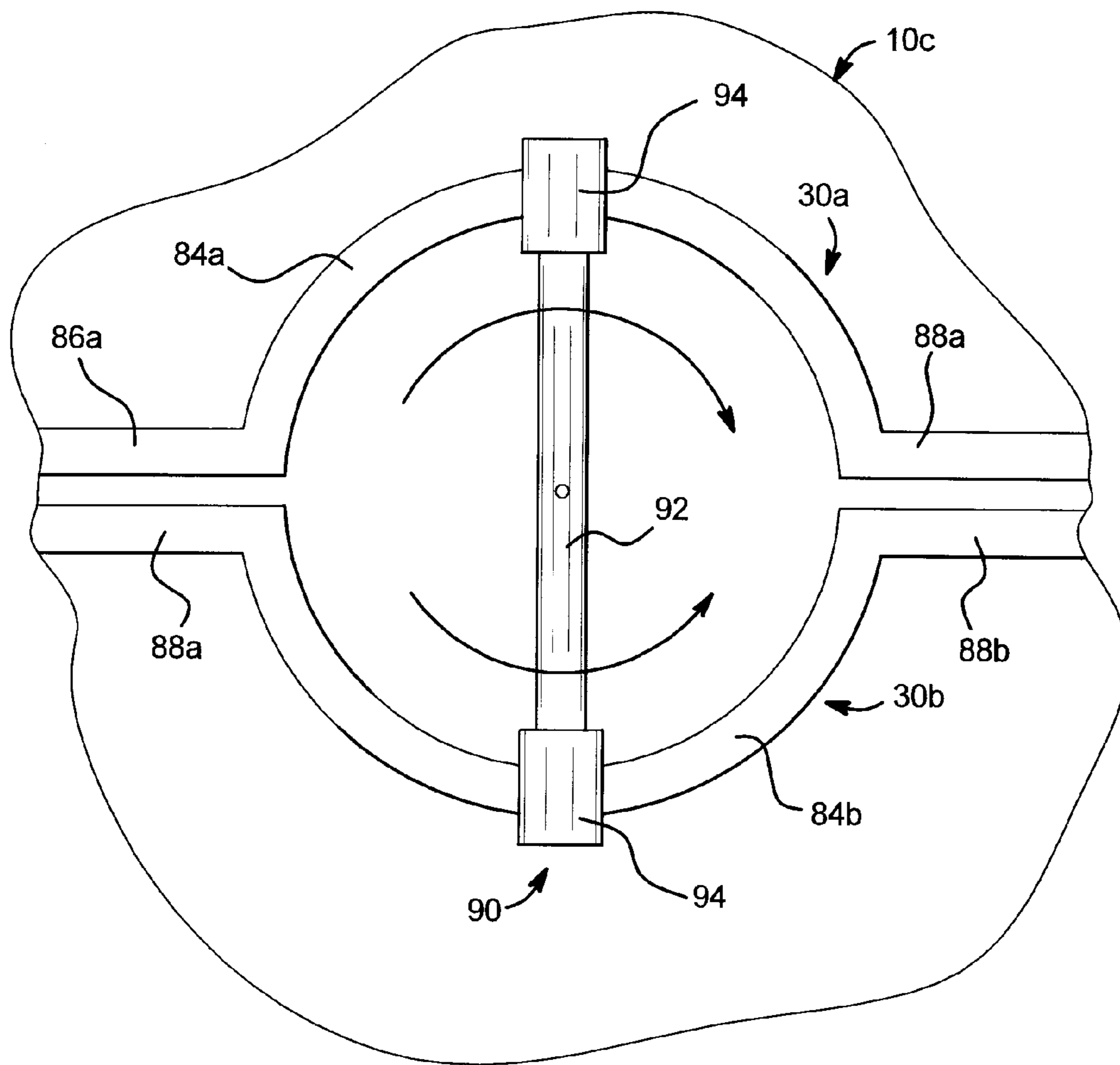


FIG. 13

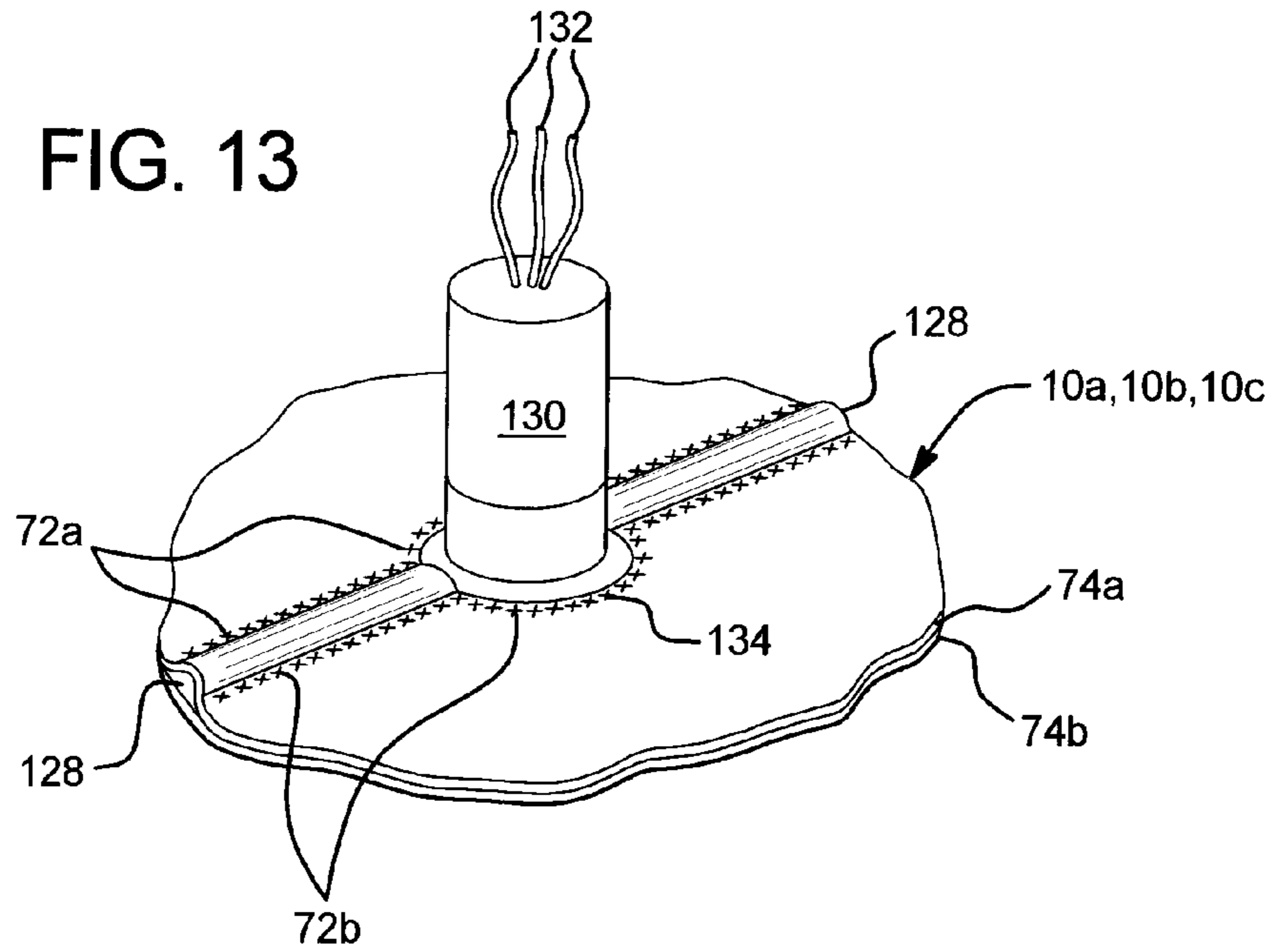


FIG. 14

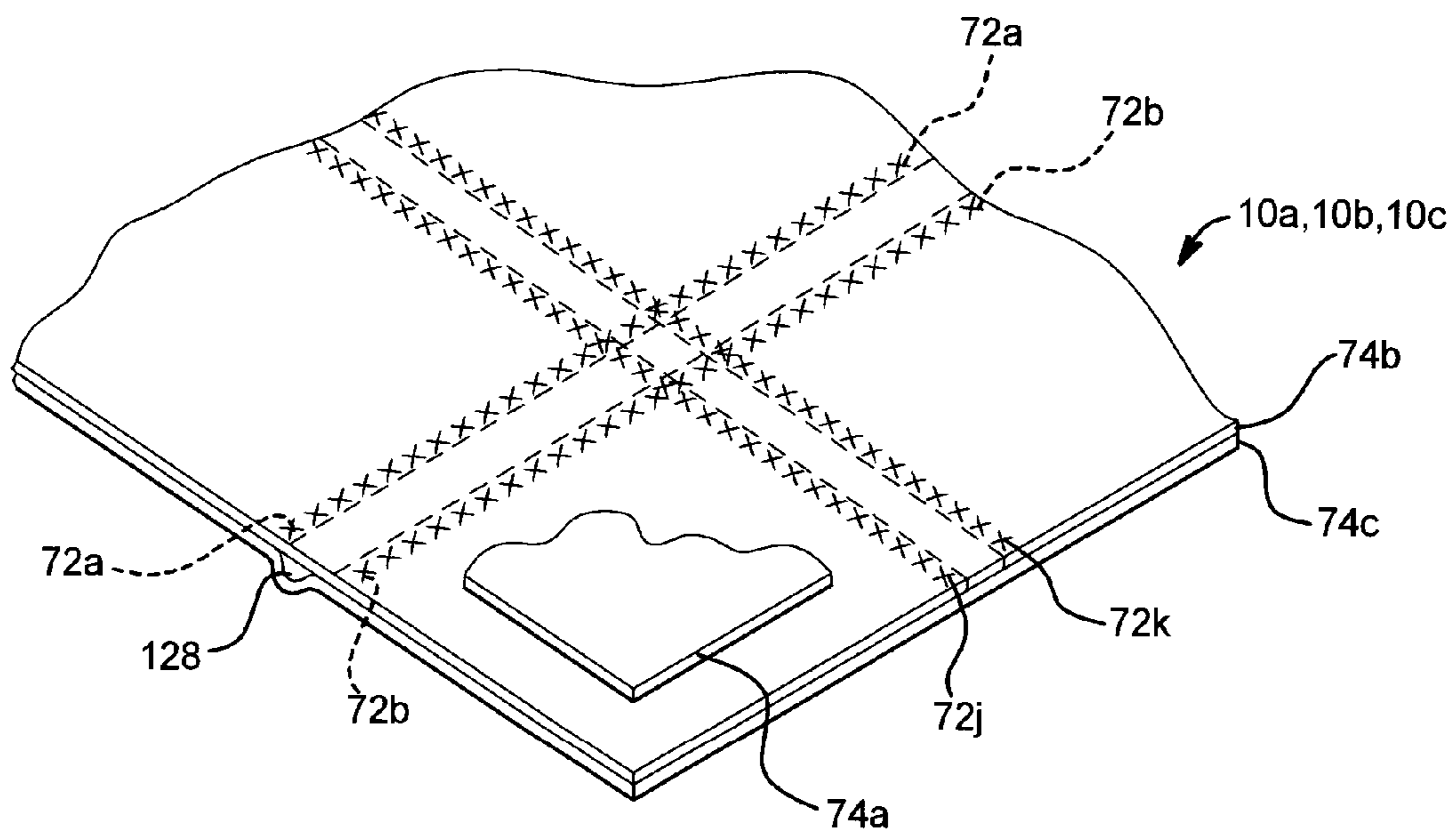


FIG. 15

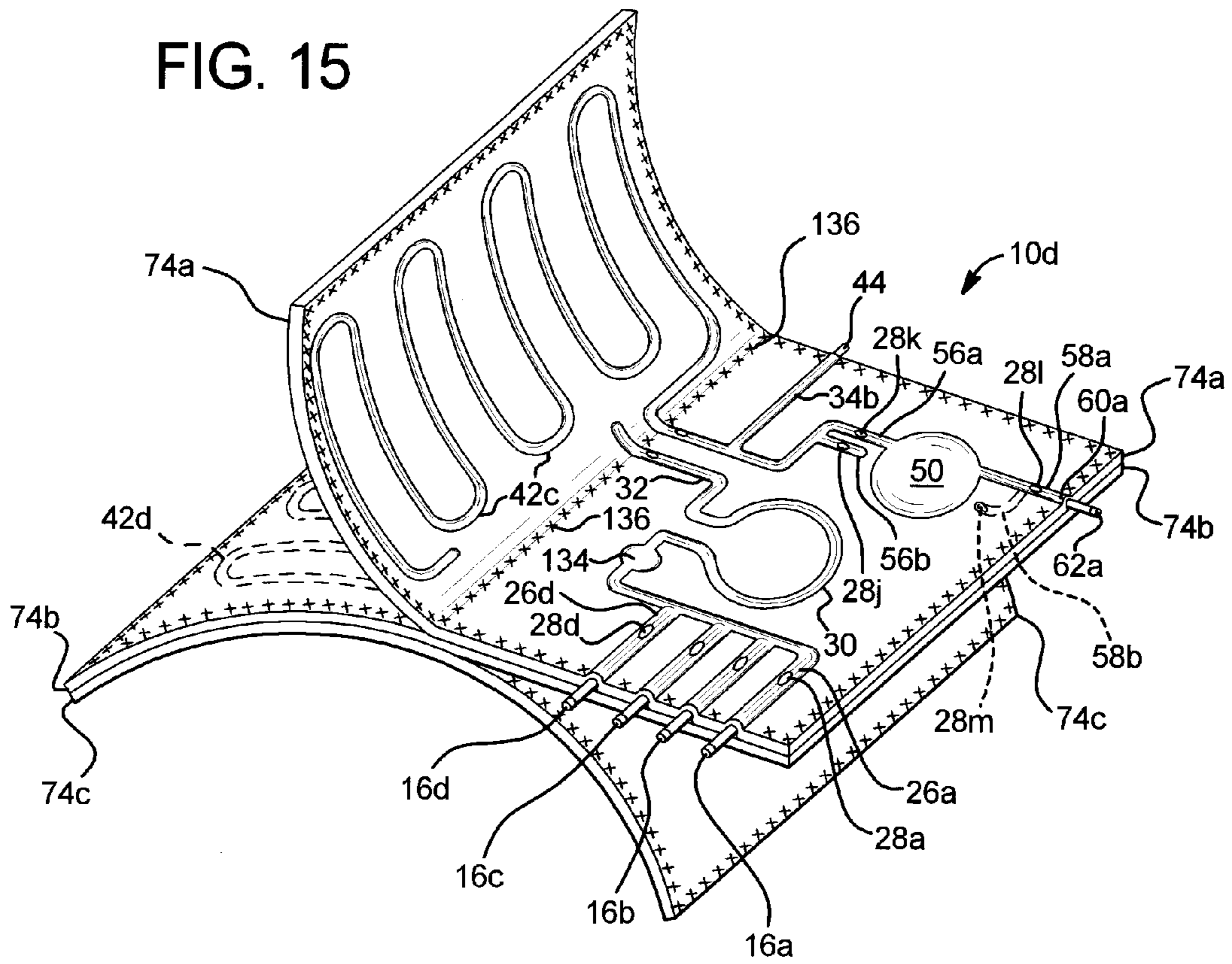


FIG. 16

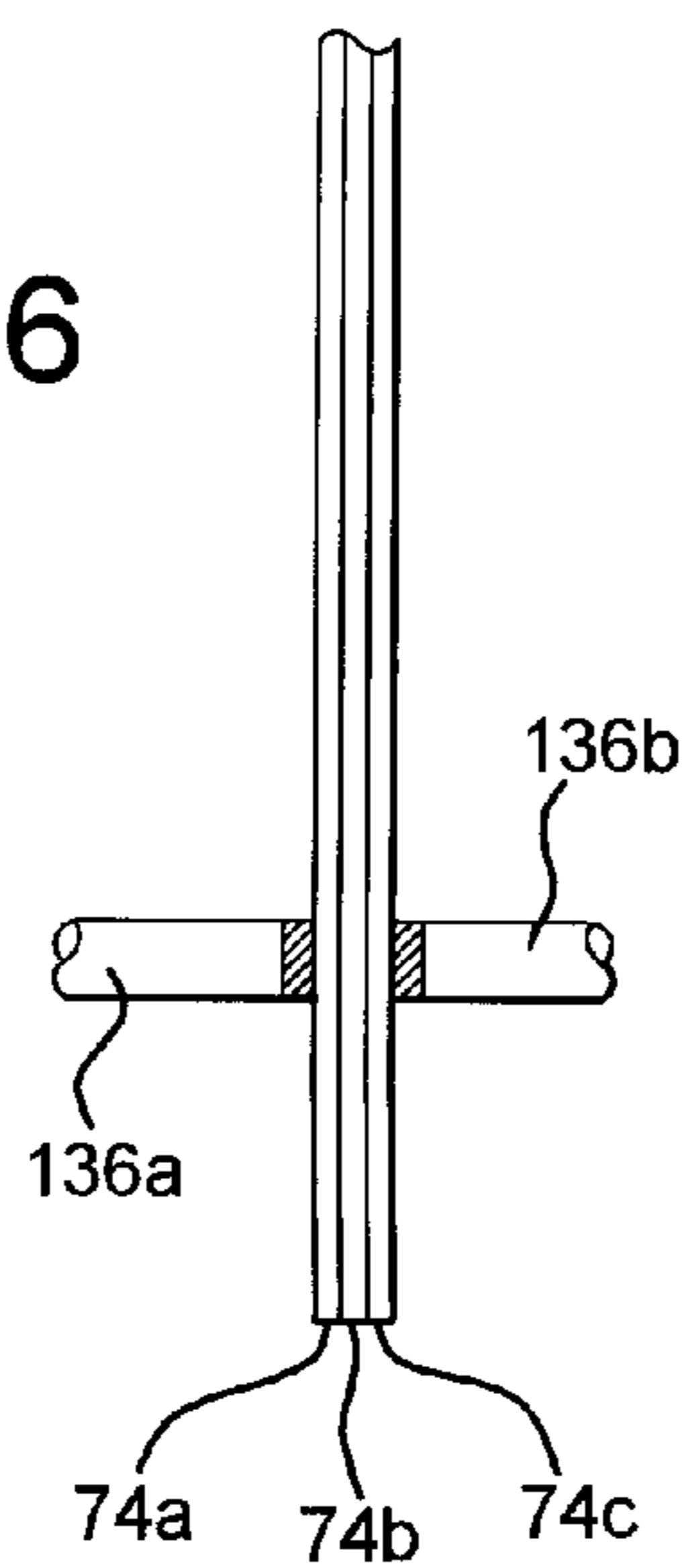


FIG. 17

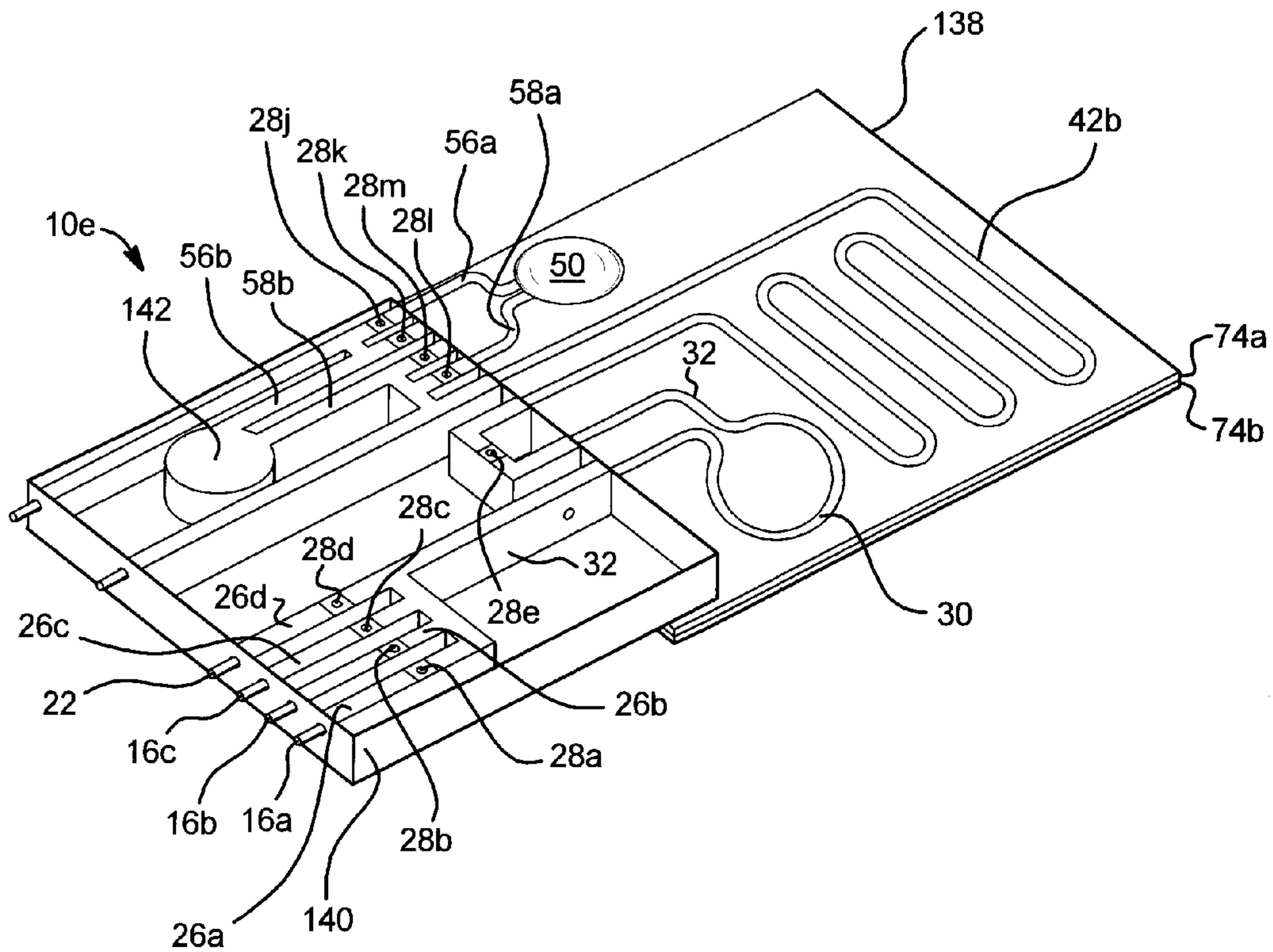


FIG. 18

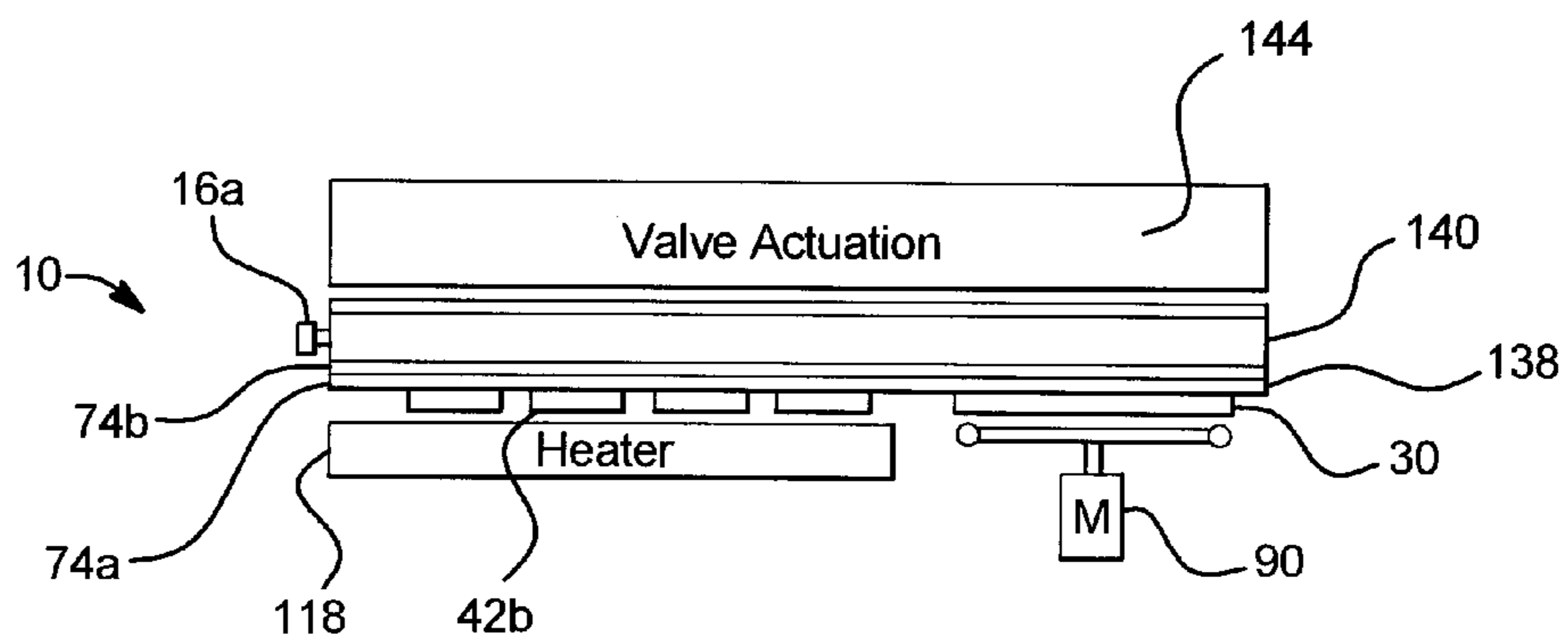


FIG. 19A

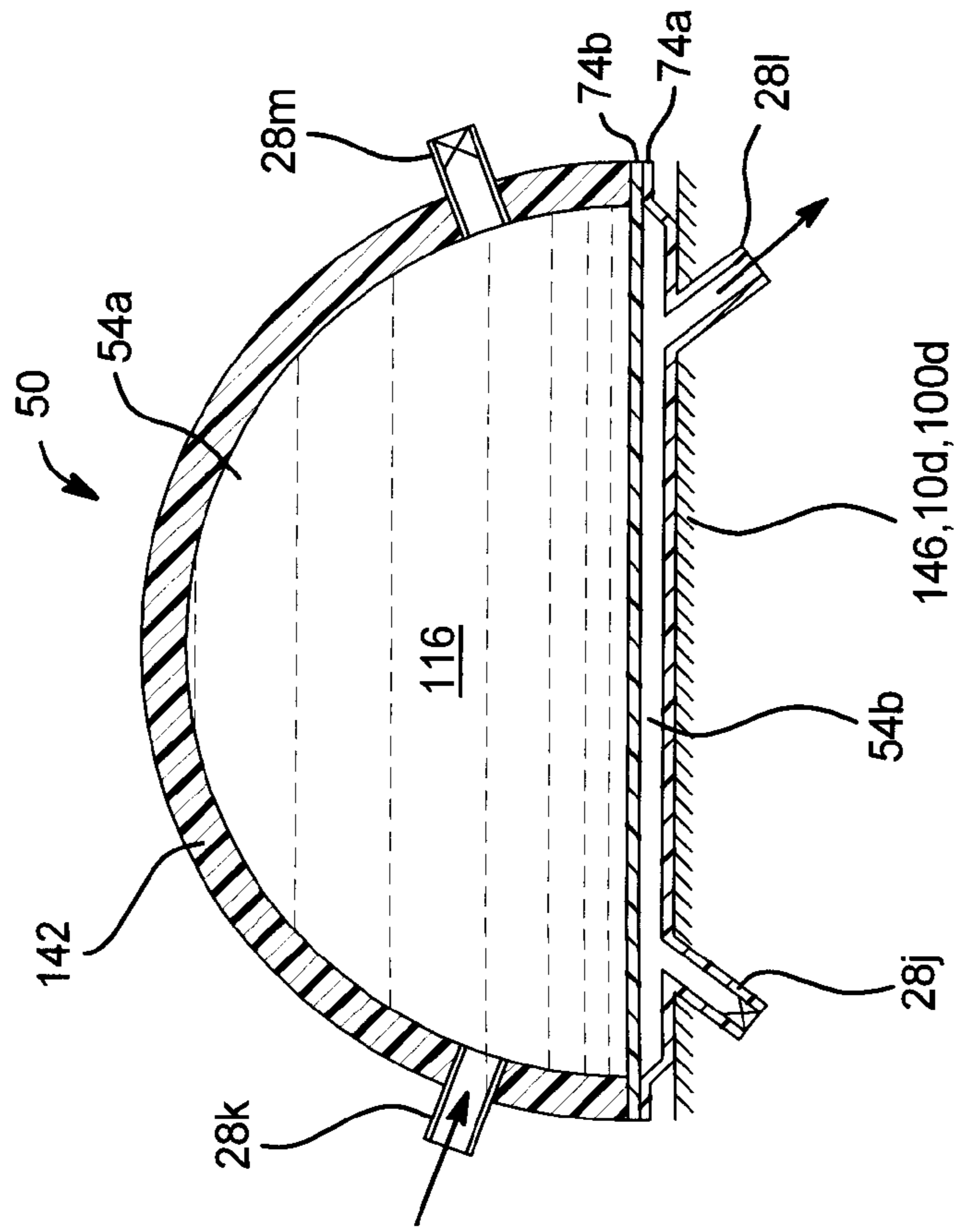


FIG. 19B

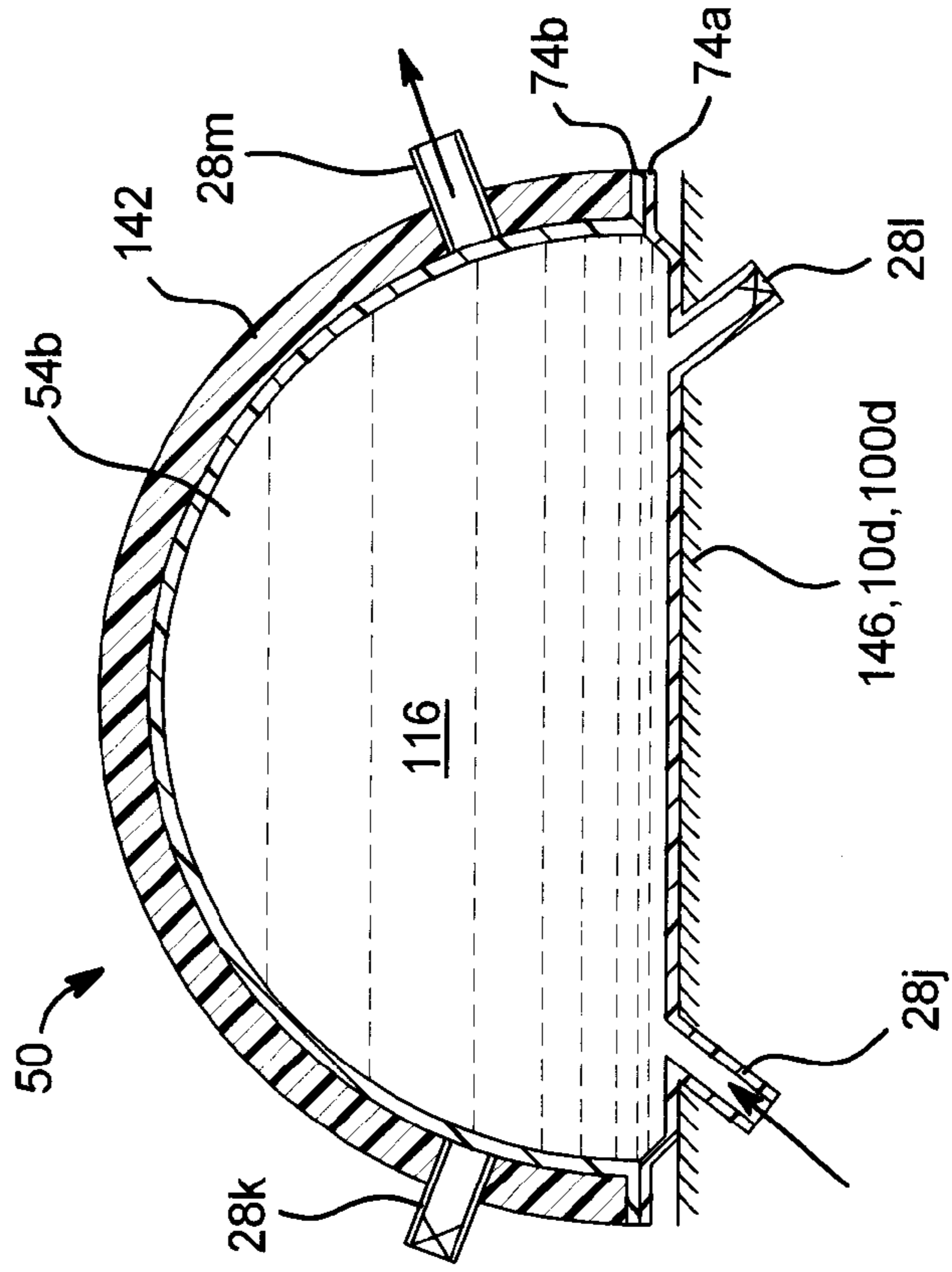


FIG. 20A

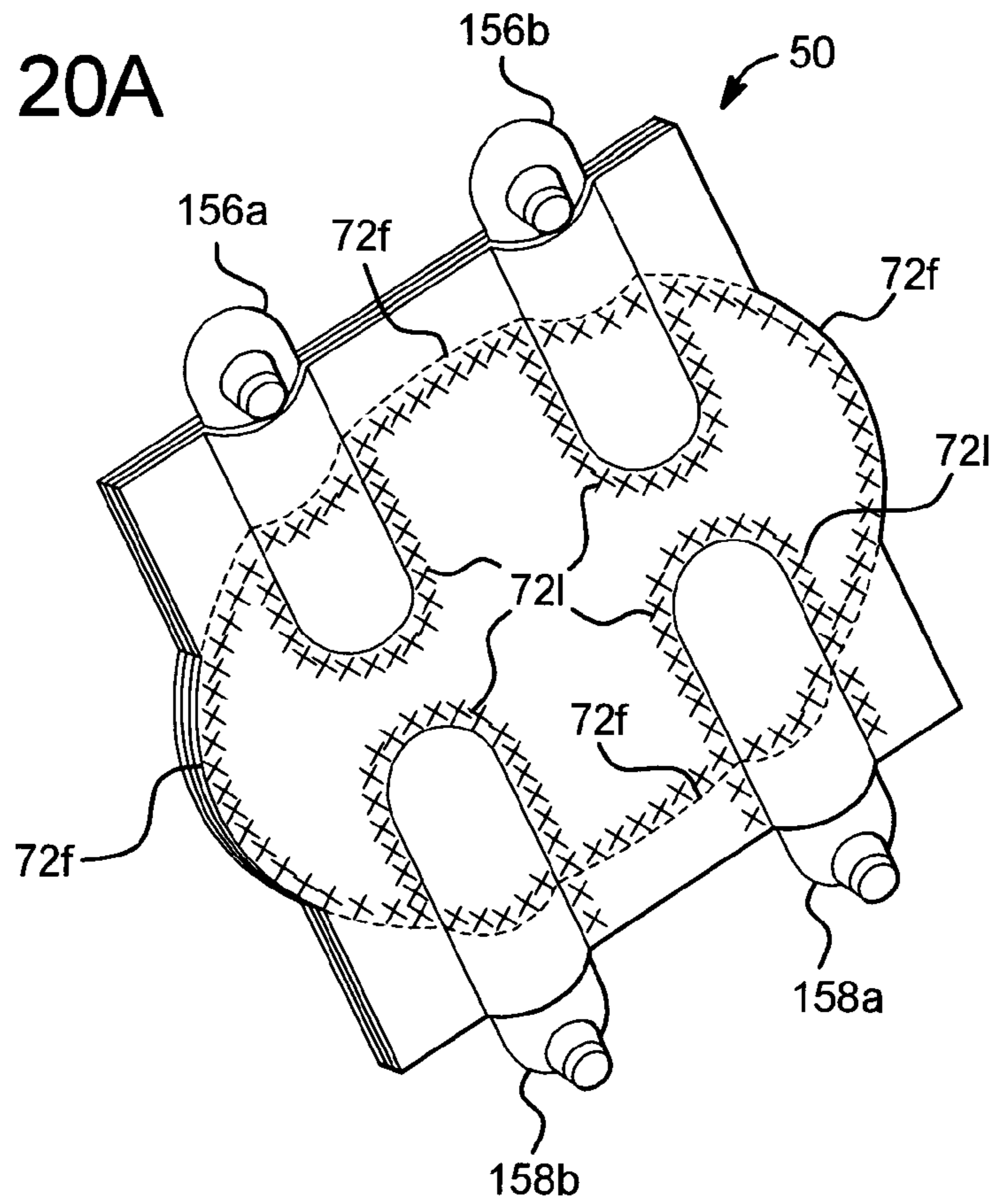


FIG. 20B

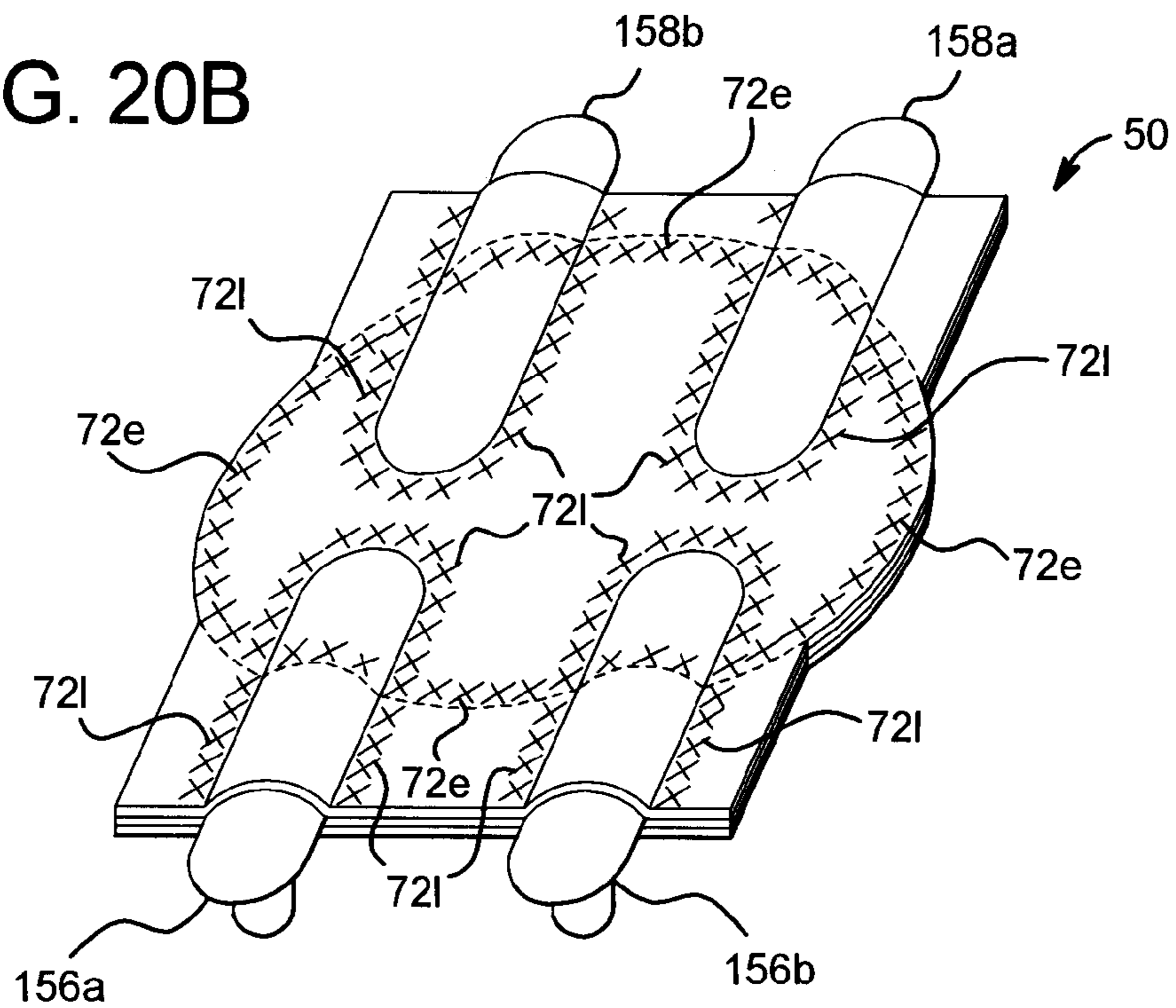


FIG. 20C

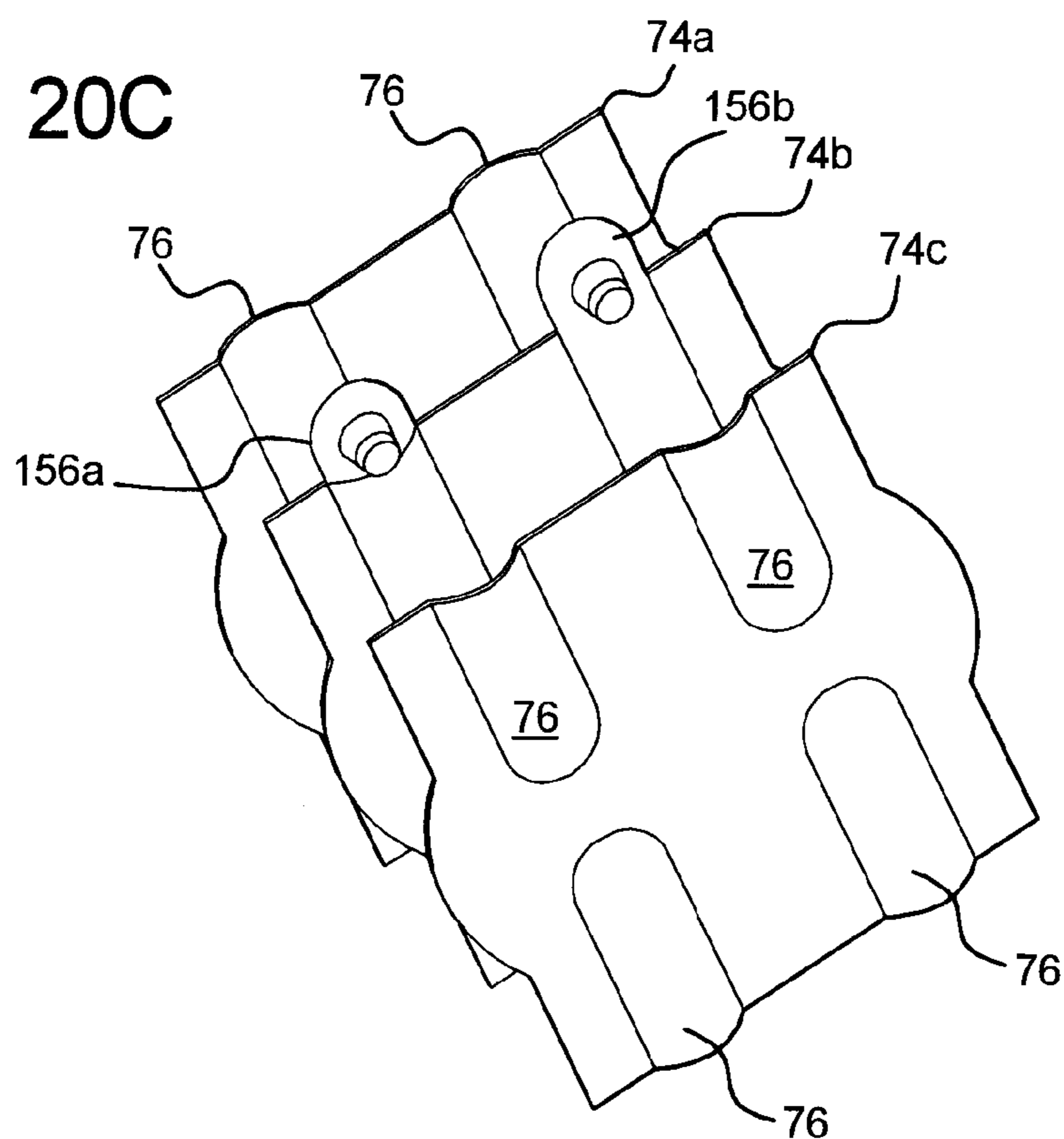
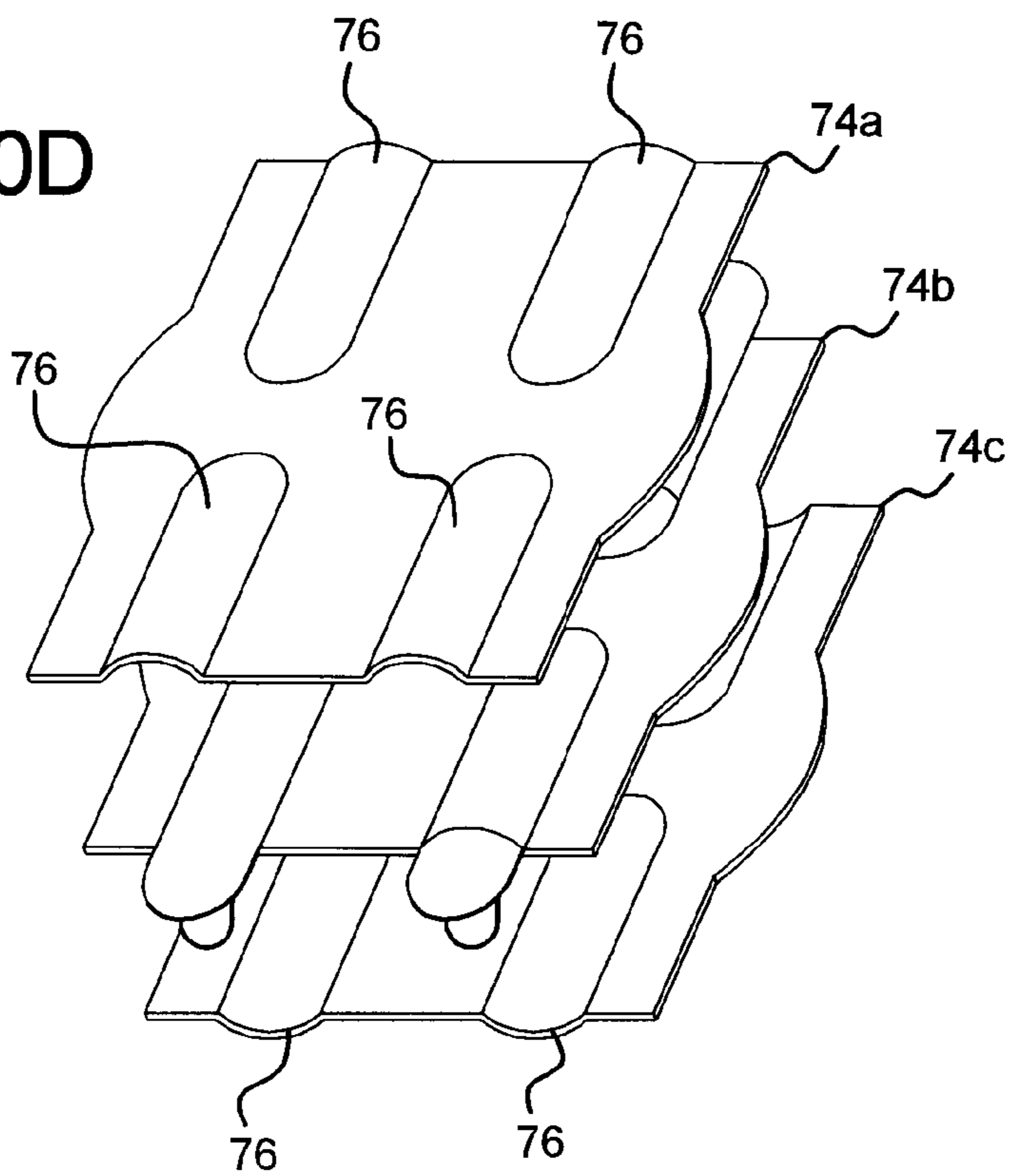


FIG. 20D



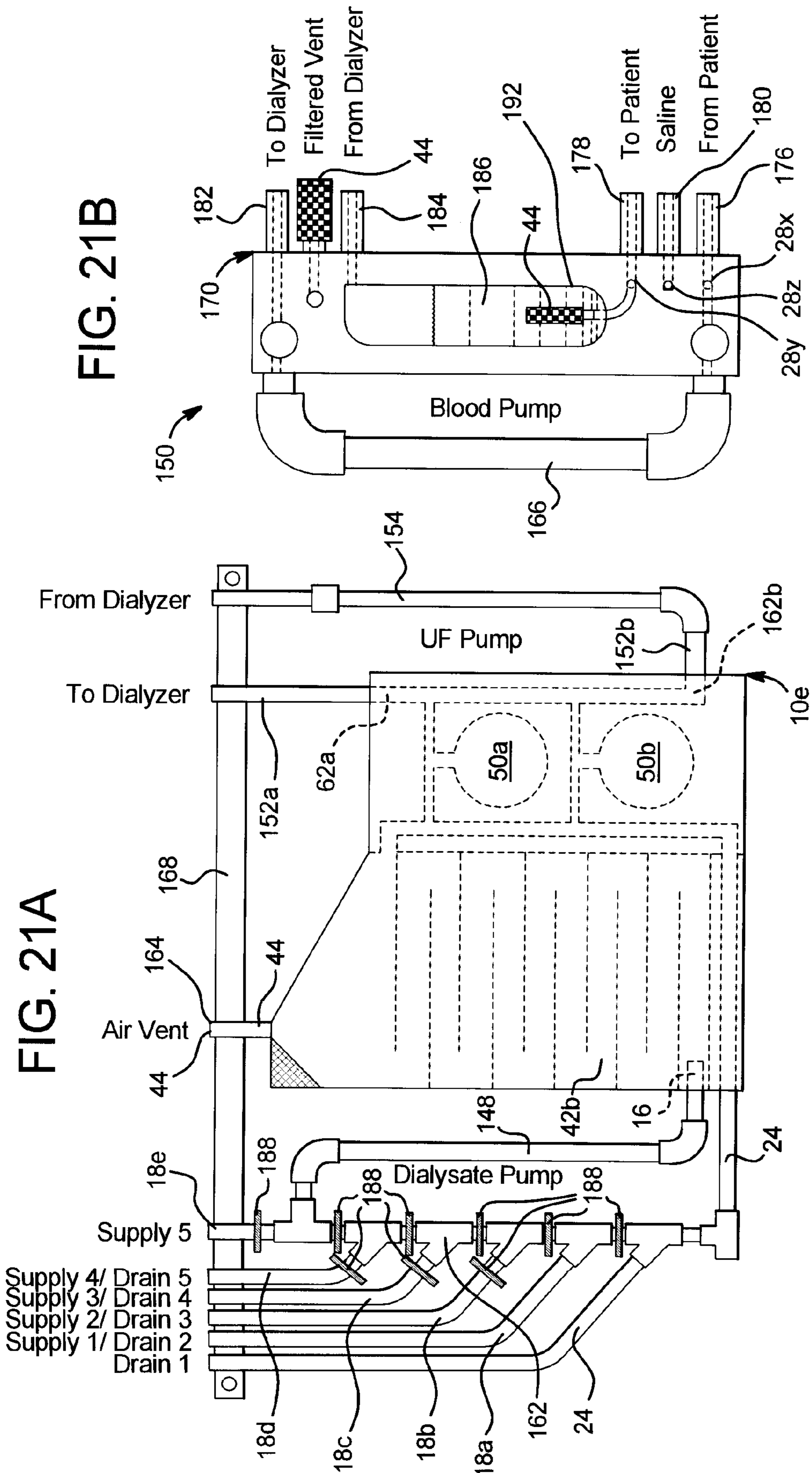


FIG. 21D

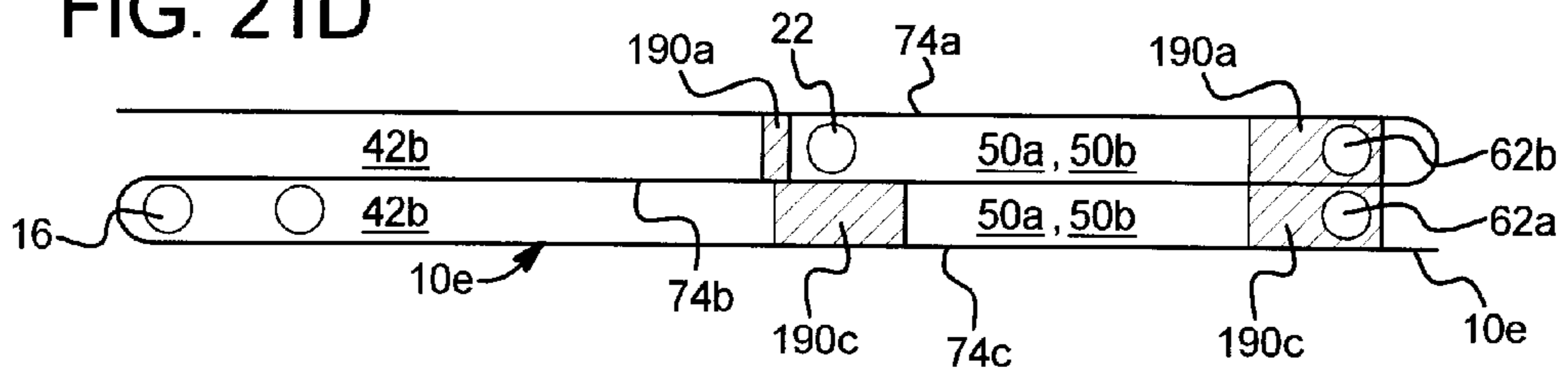


FIG. 21C

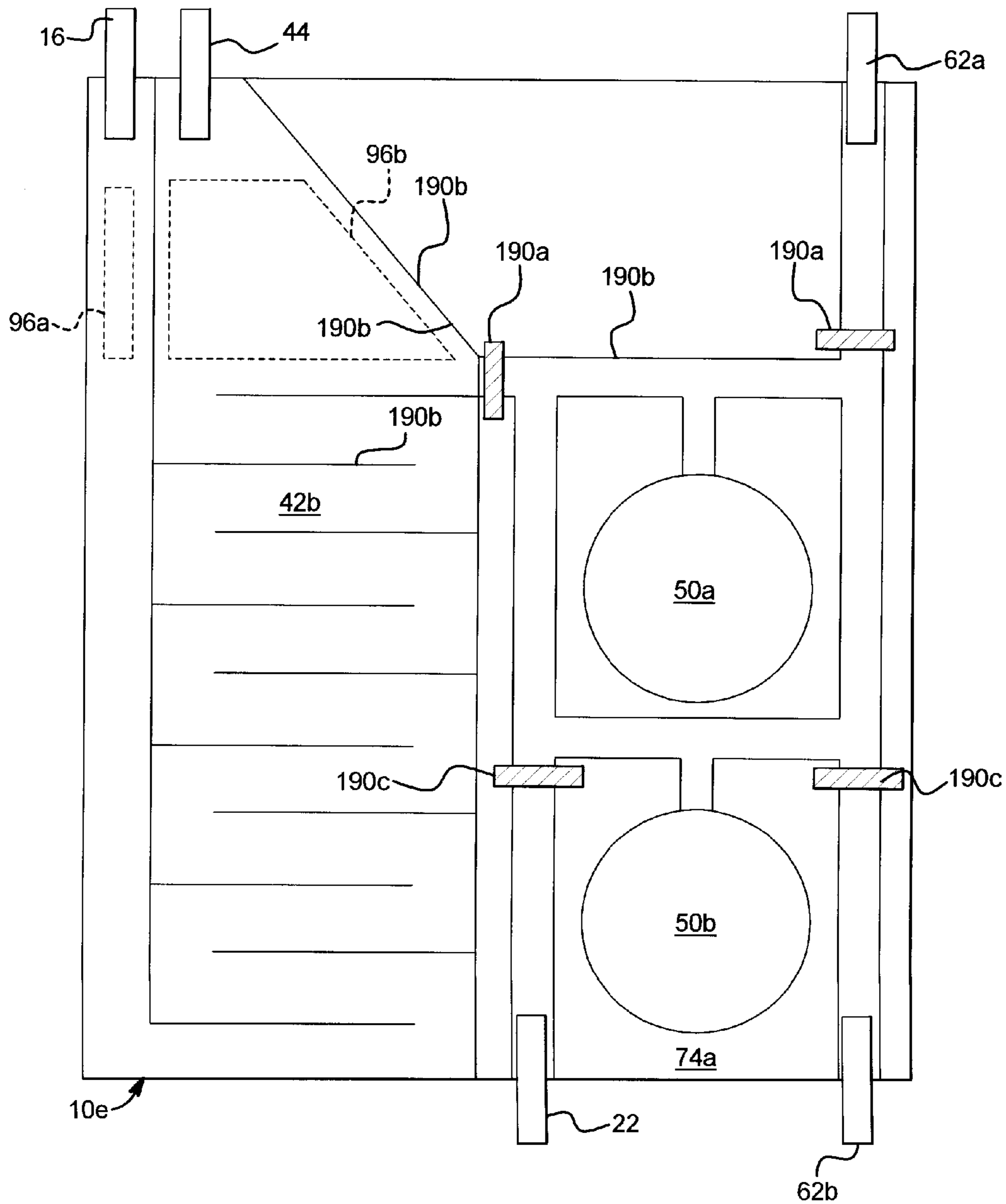
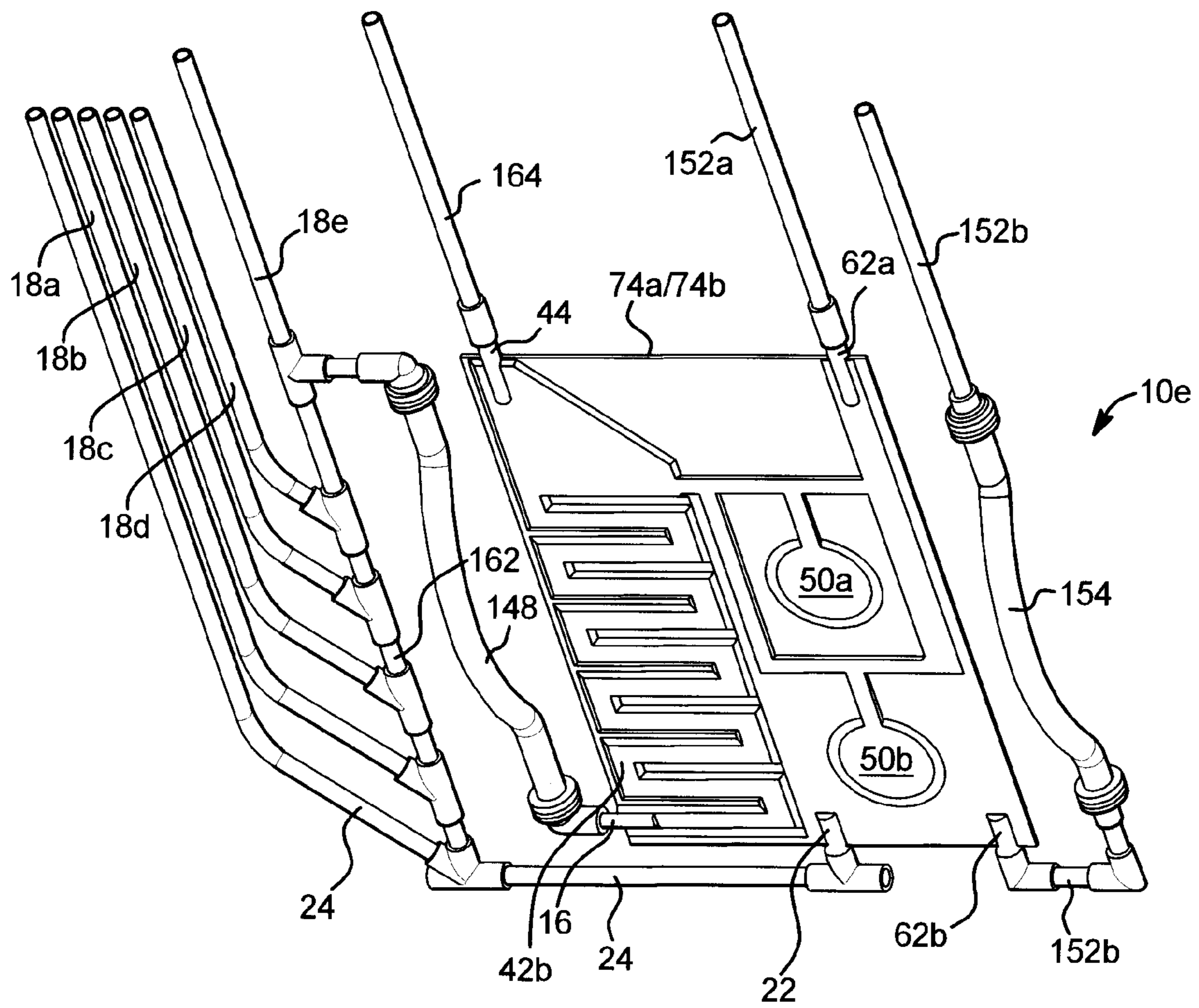
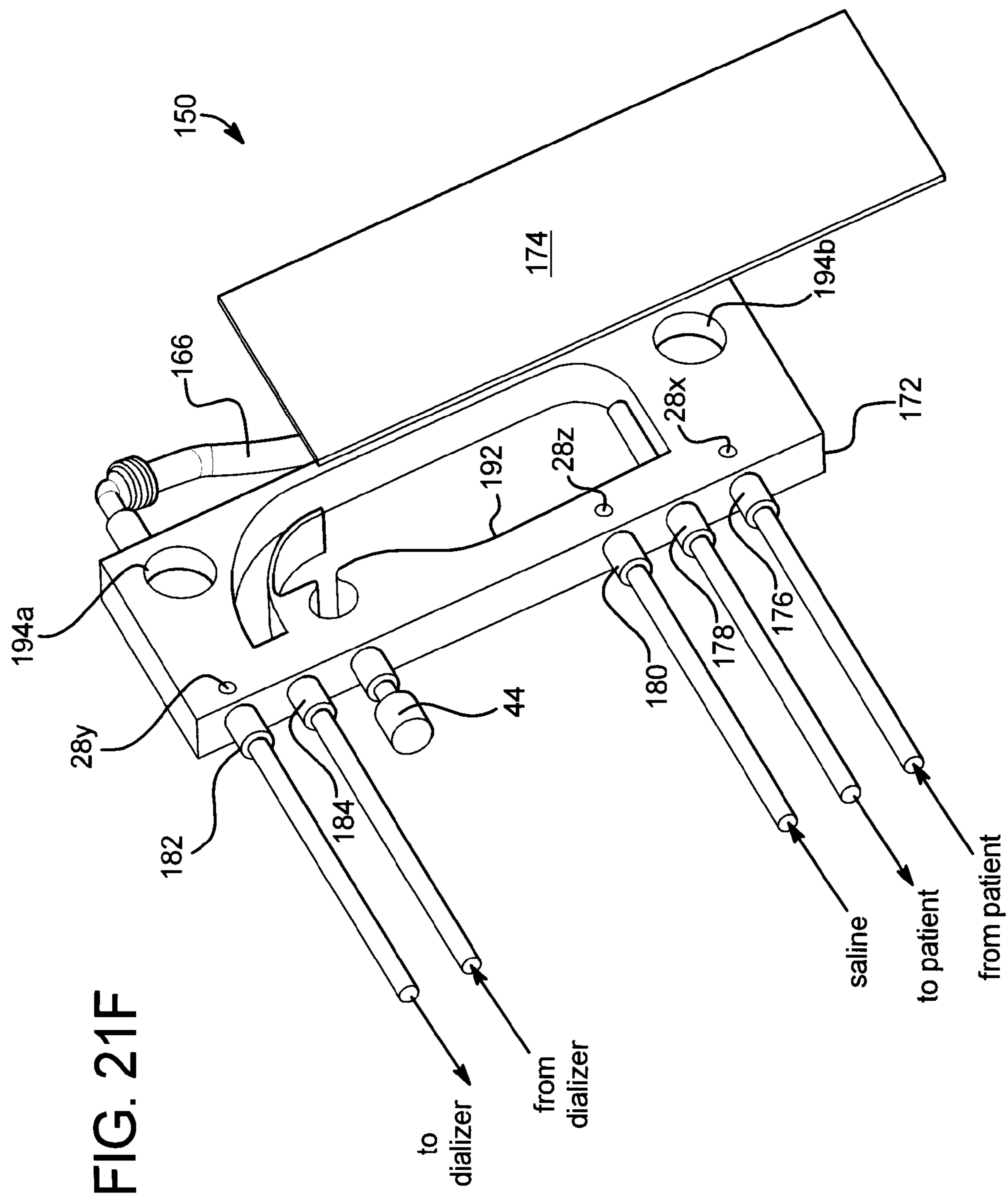


FIG. 21E





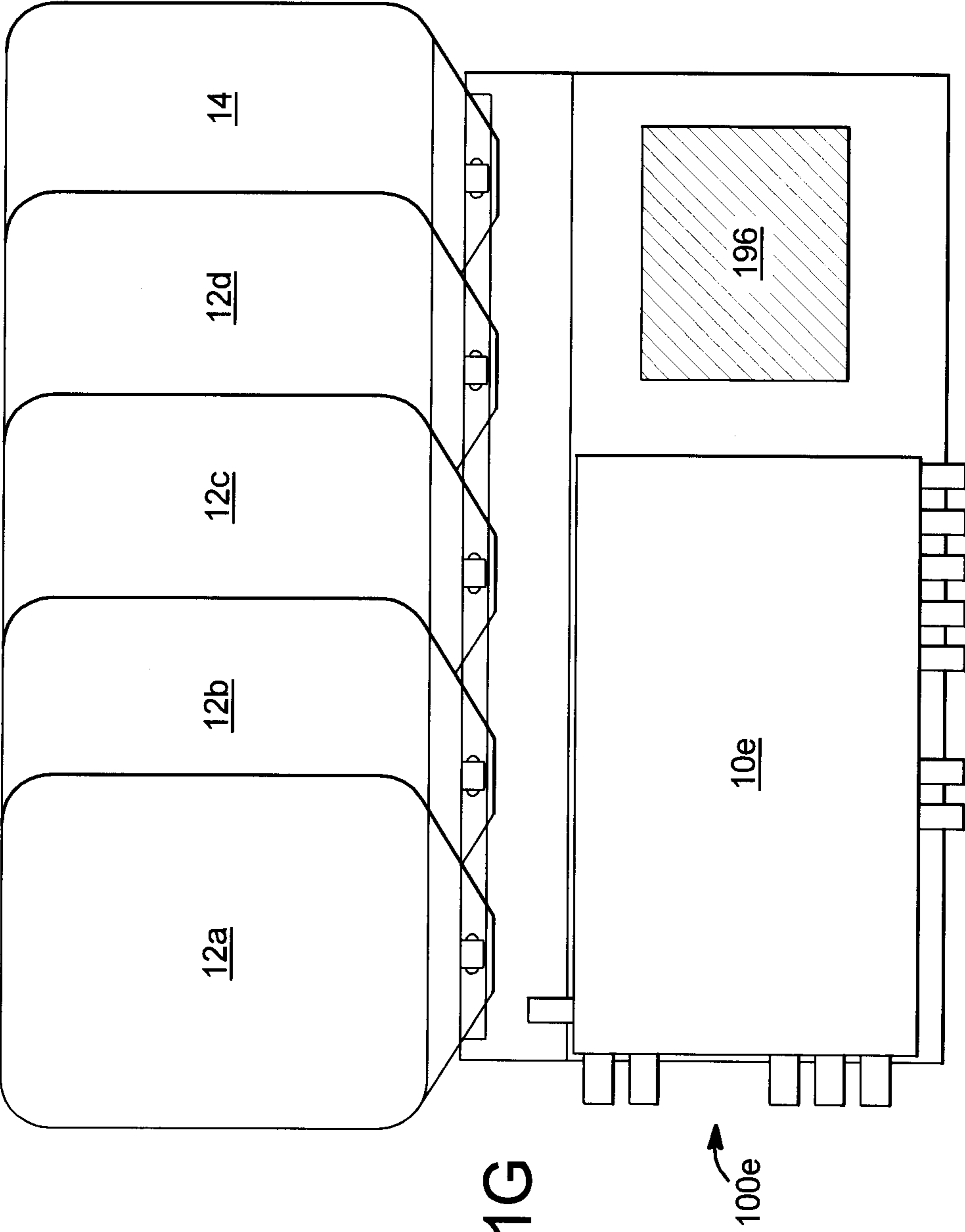


FIG. 21G

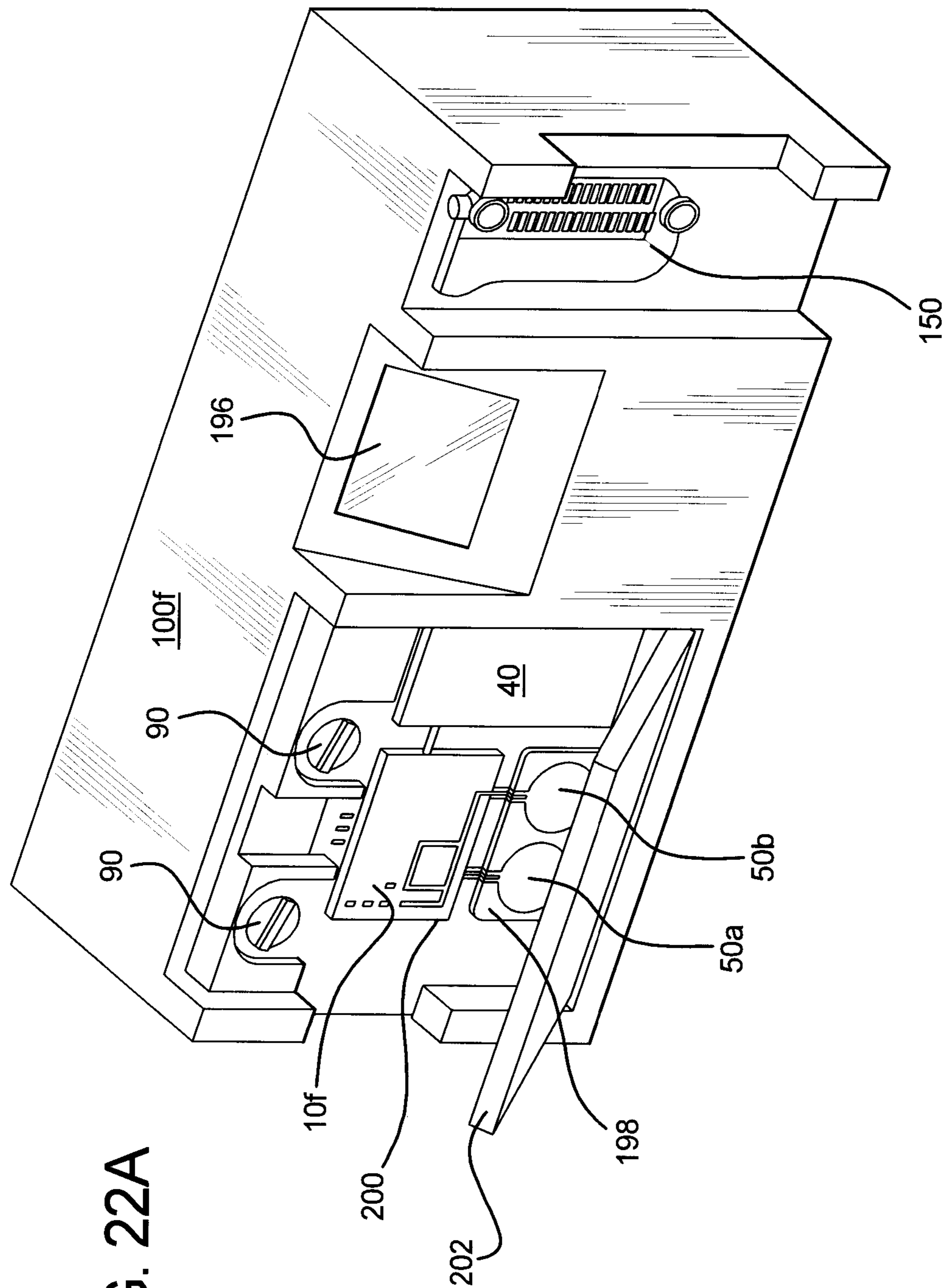


FIG. 22A

FIG. 22B

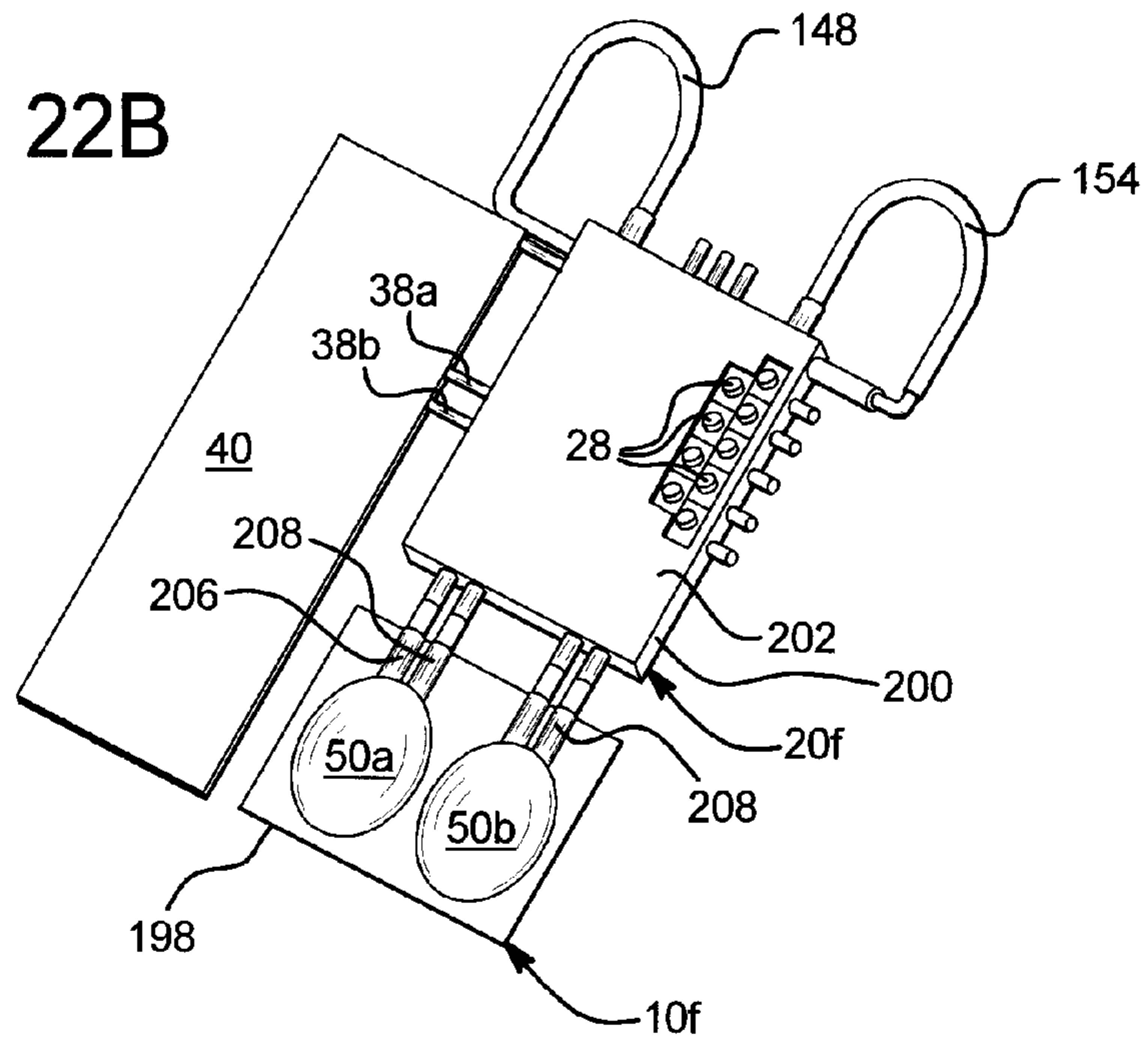


FIG. 22C

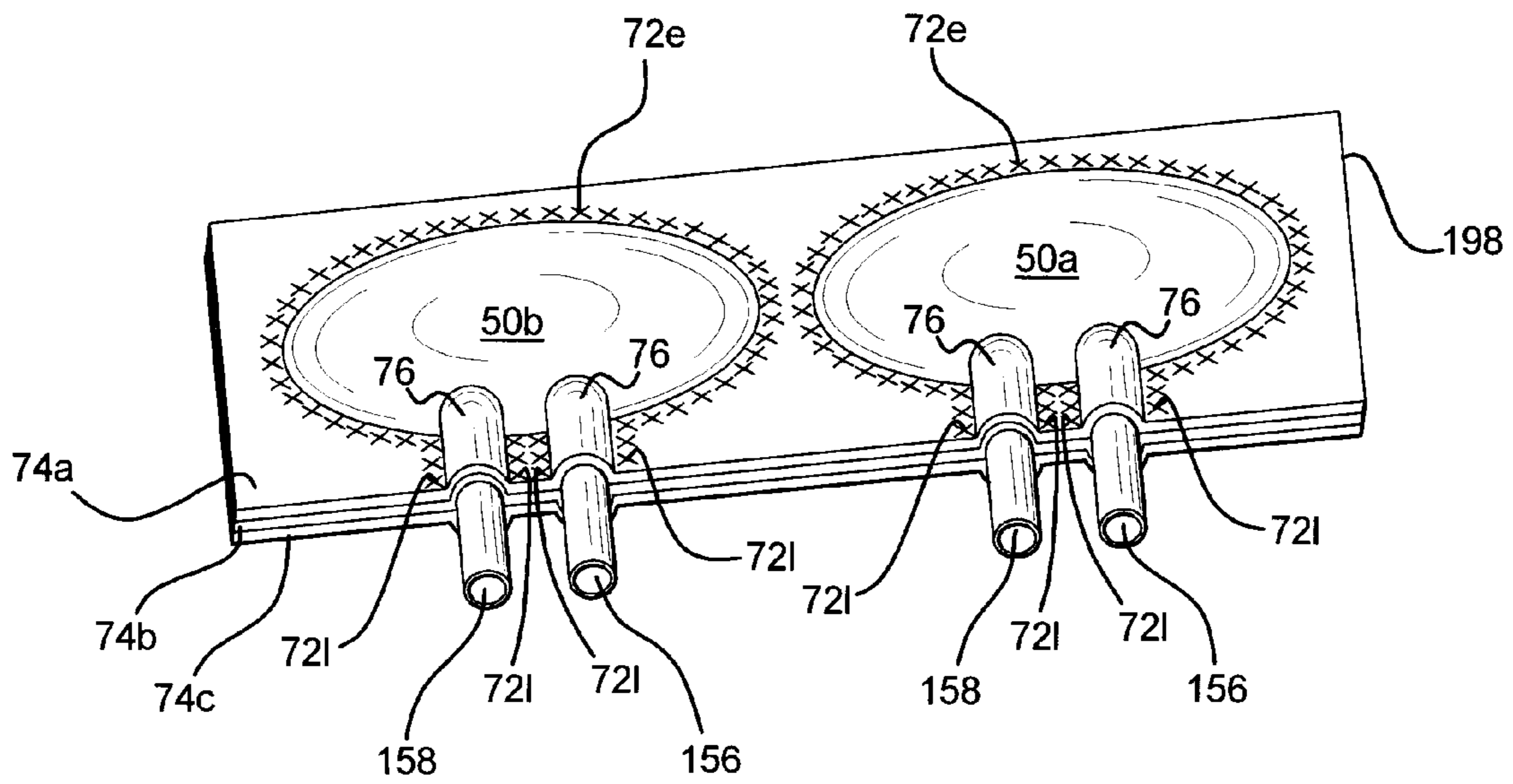


FIG. 22D

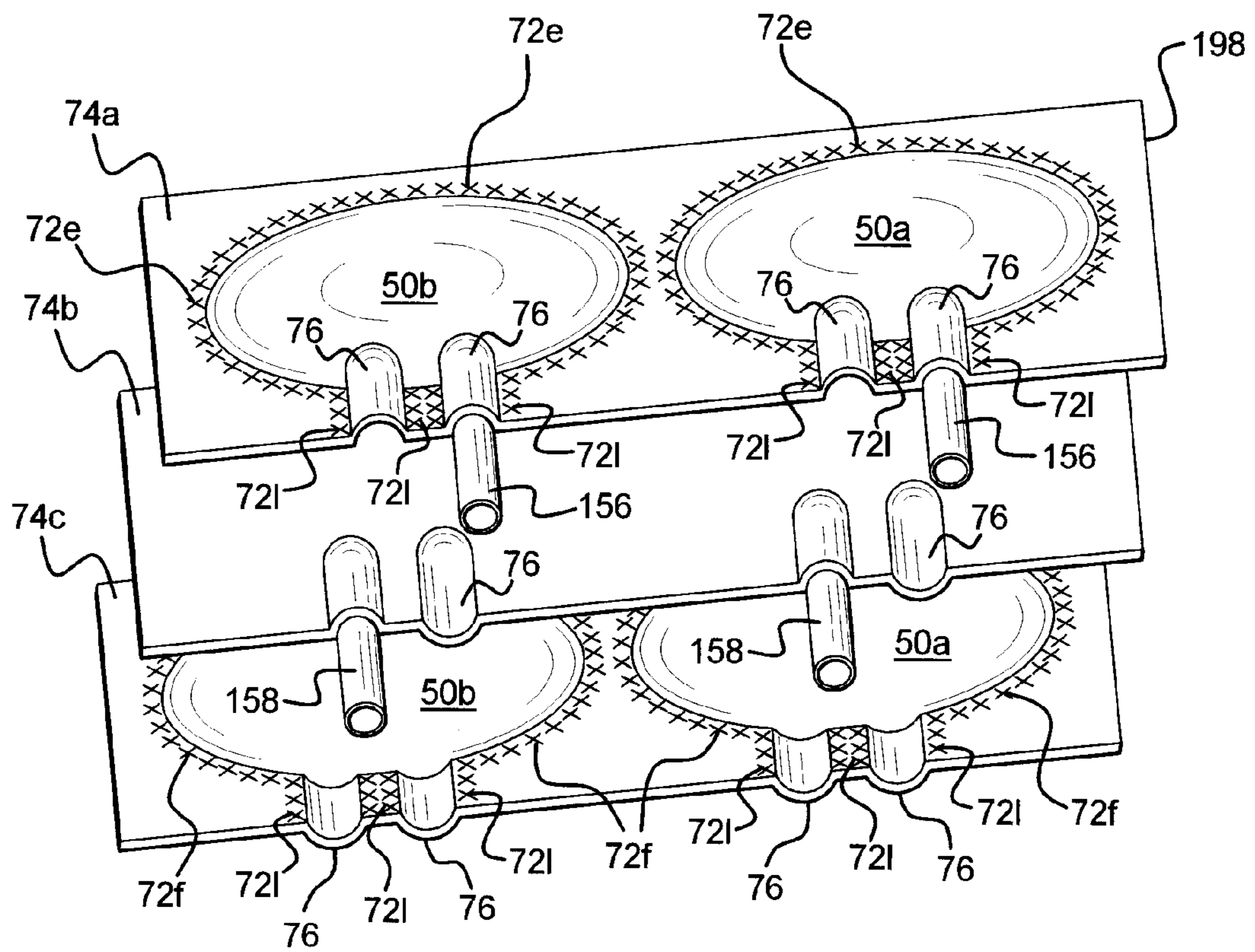


FIG. 23

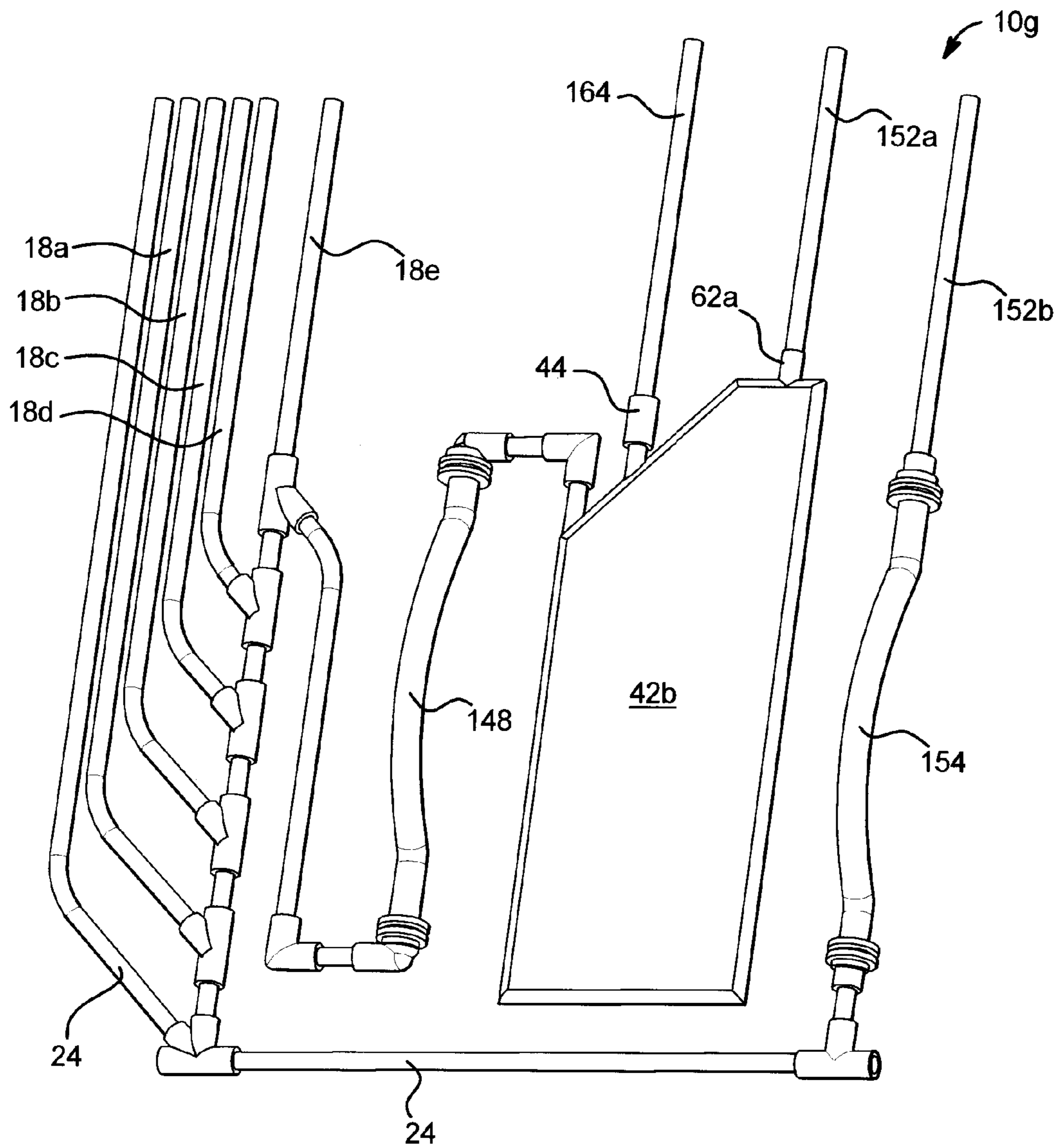


FIG. 24A

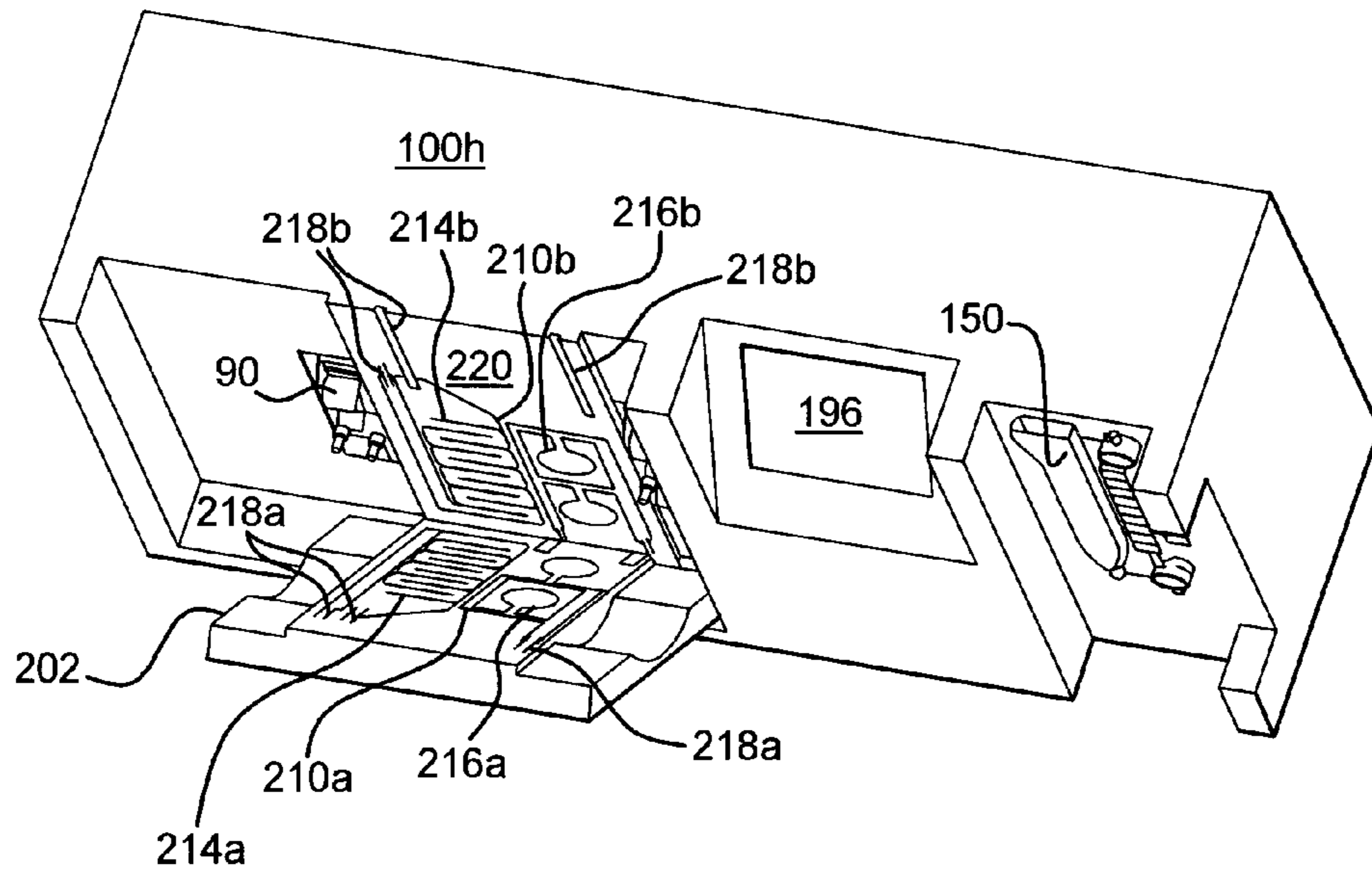


FIG. 24B

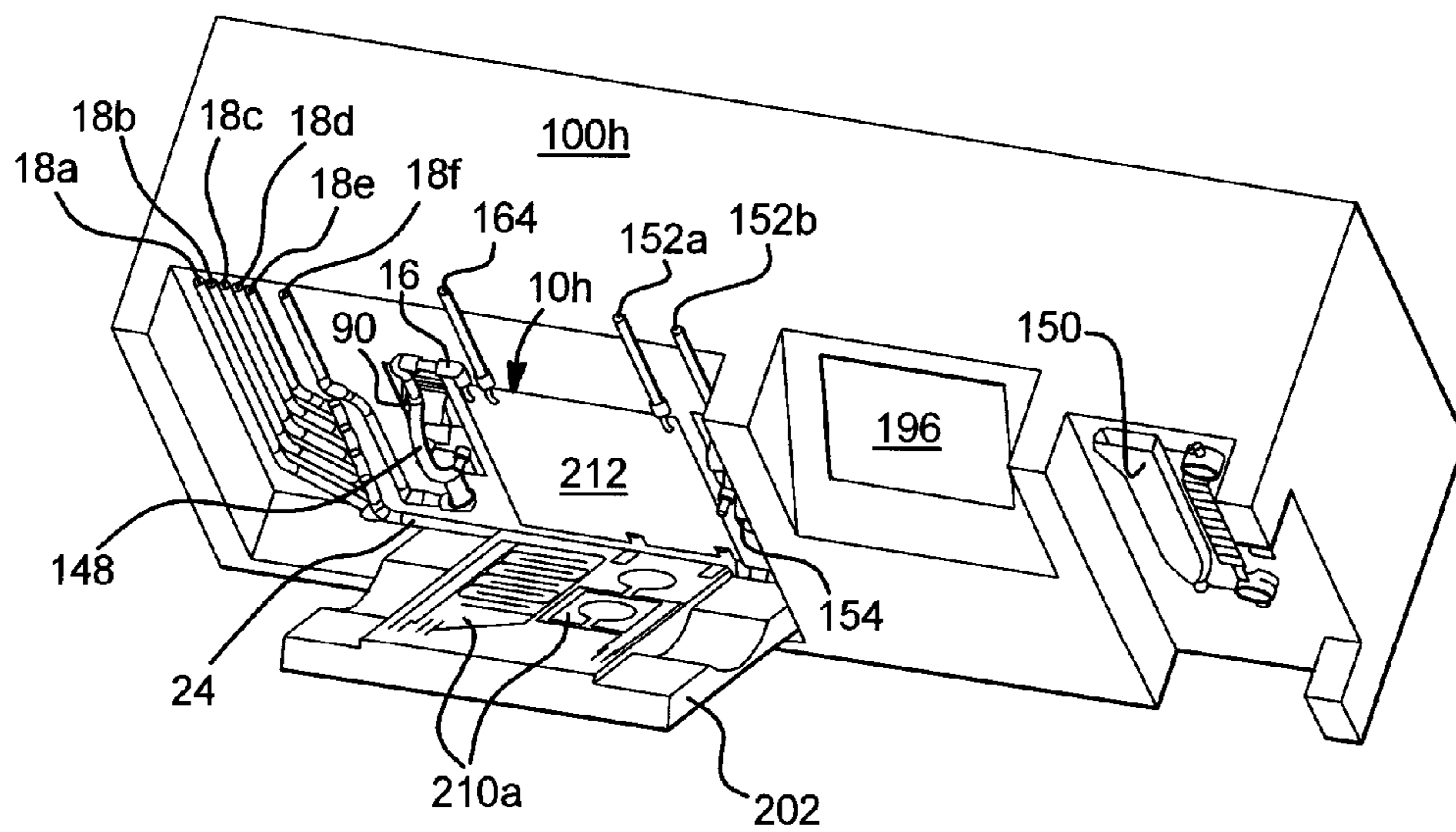


FIG.25A

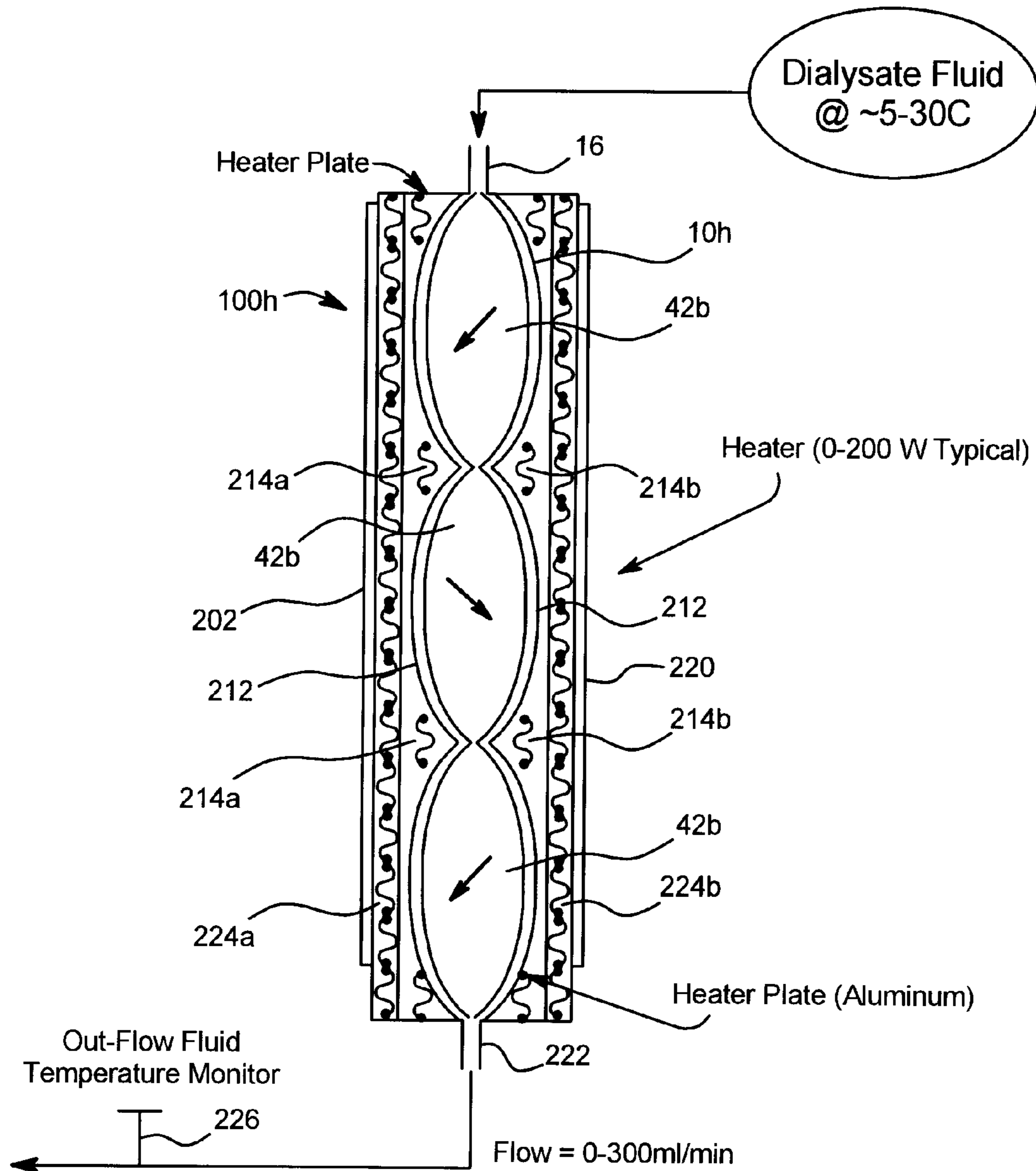


FIG. 25B

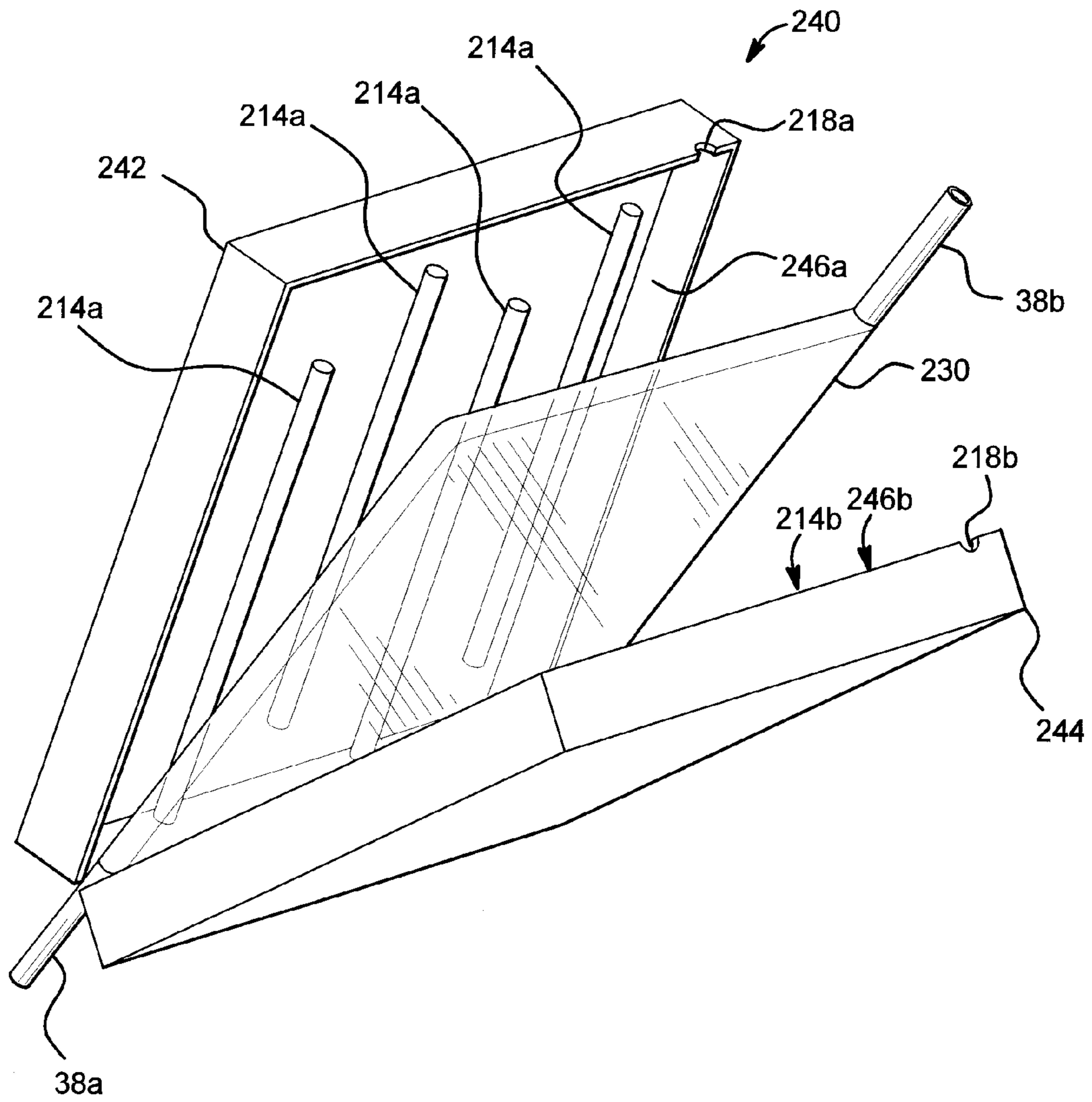


FIG. 26A

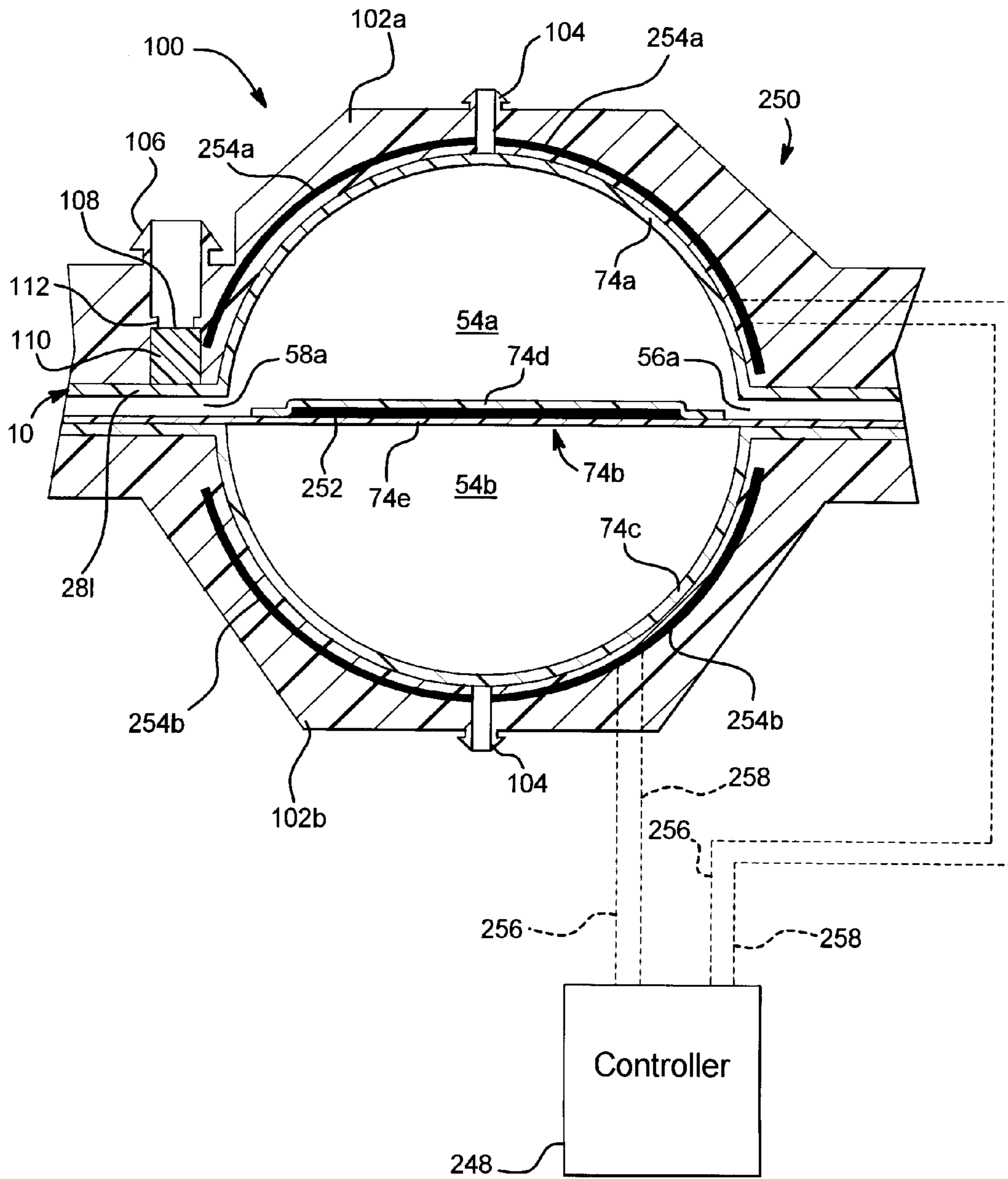


FIG. 26B

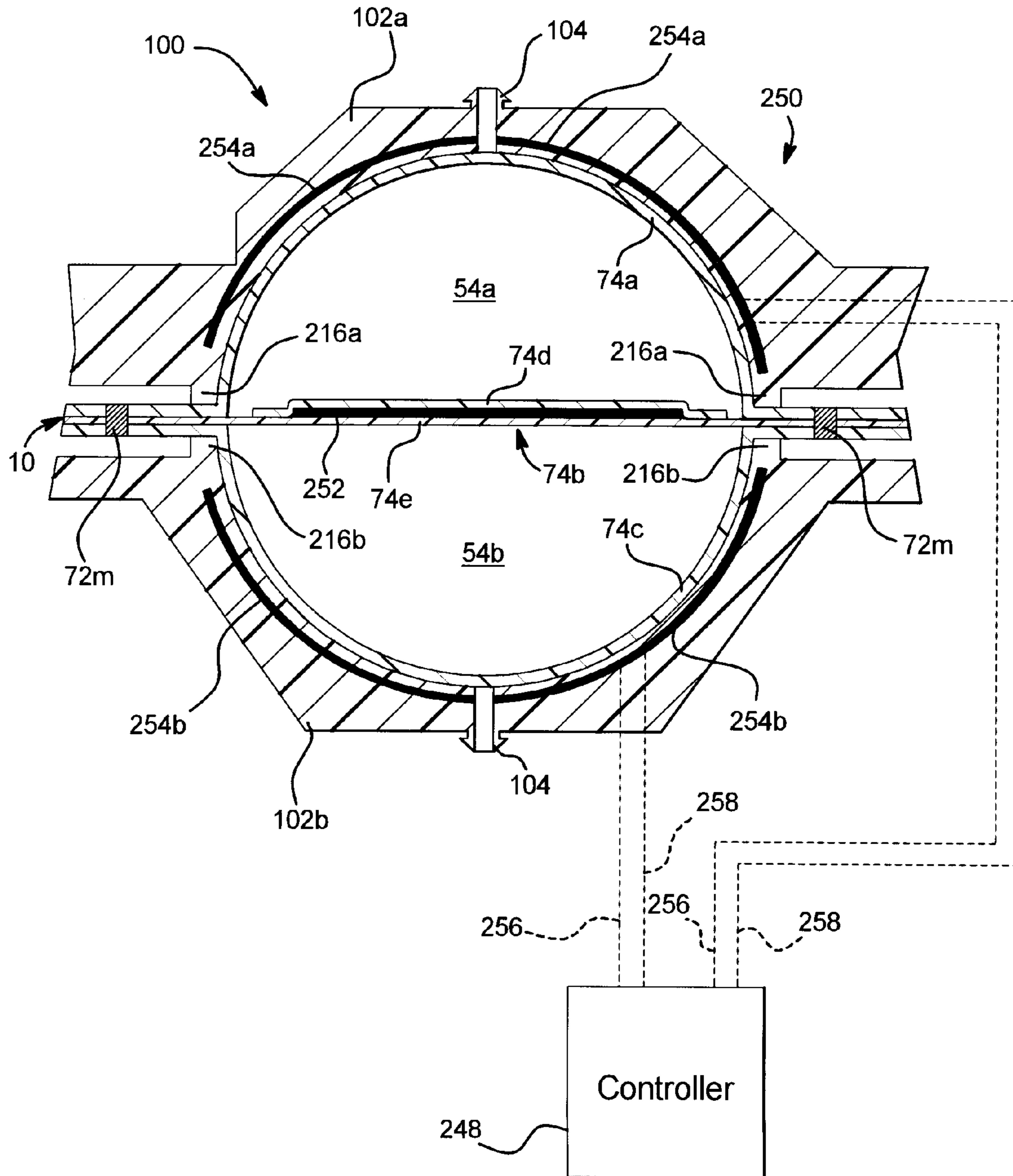
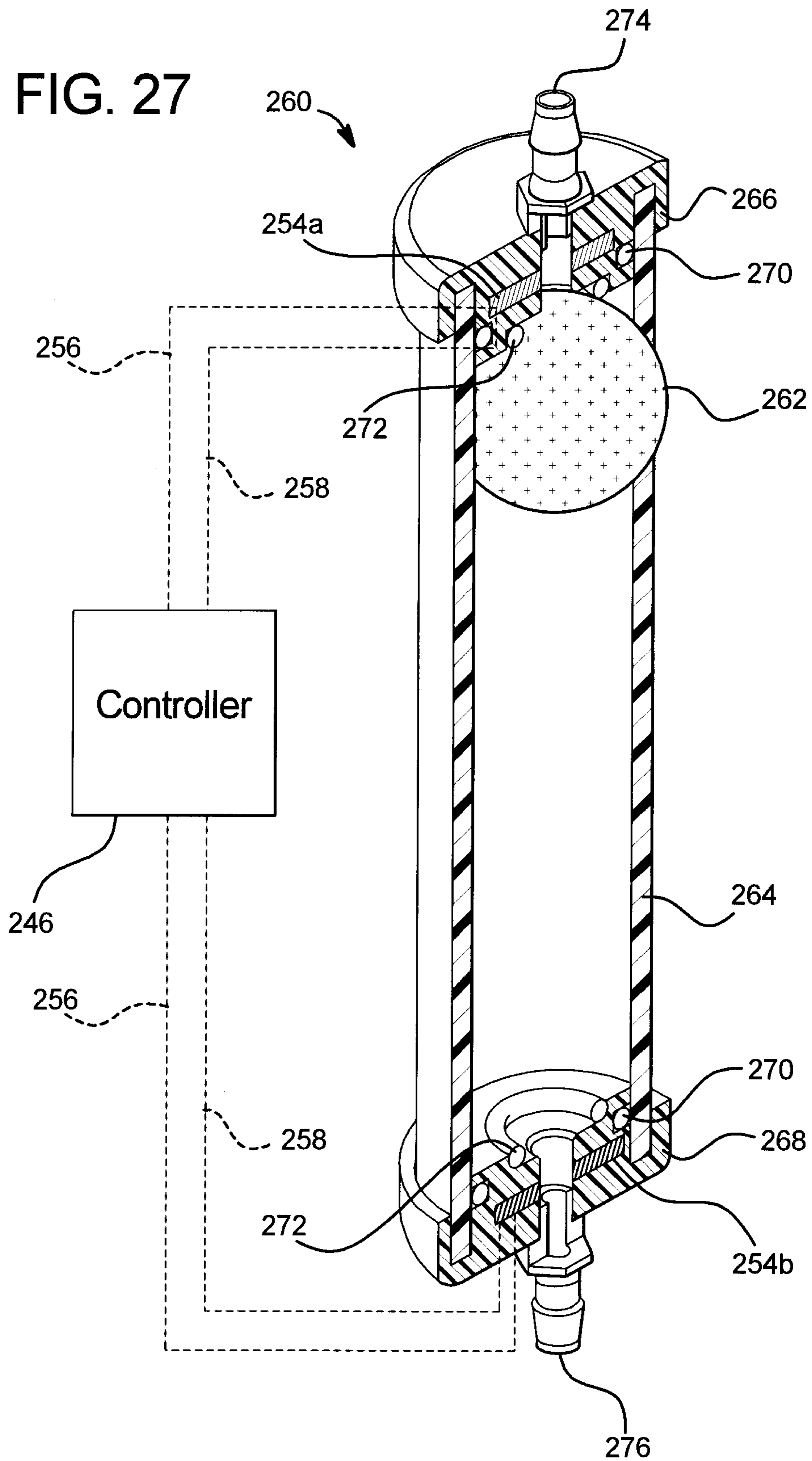


FIG. 27



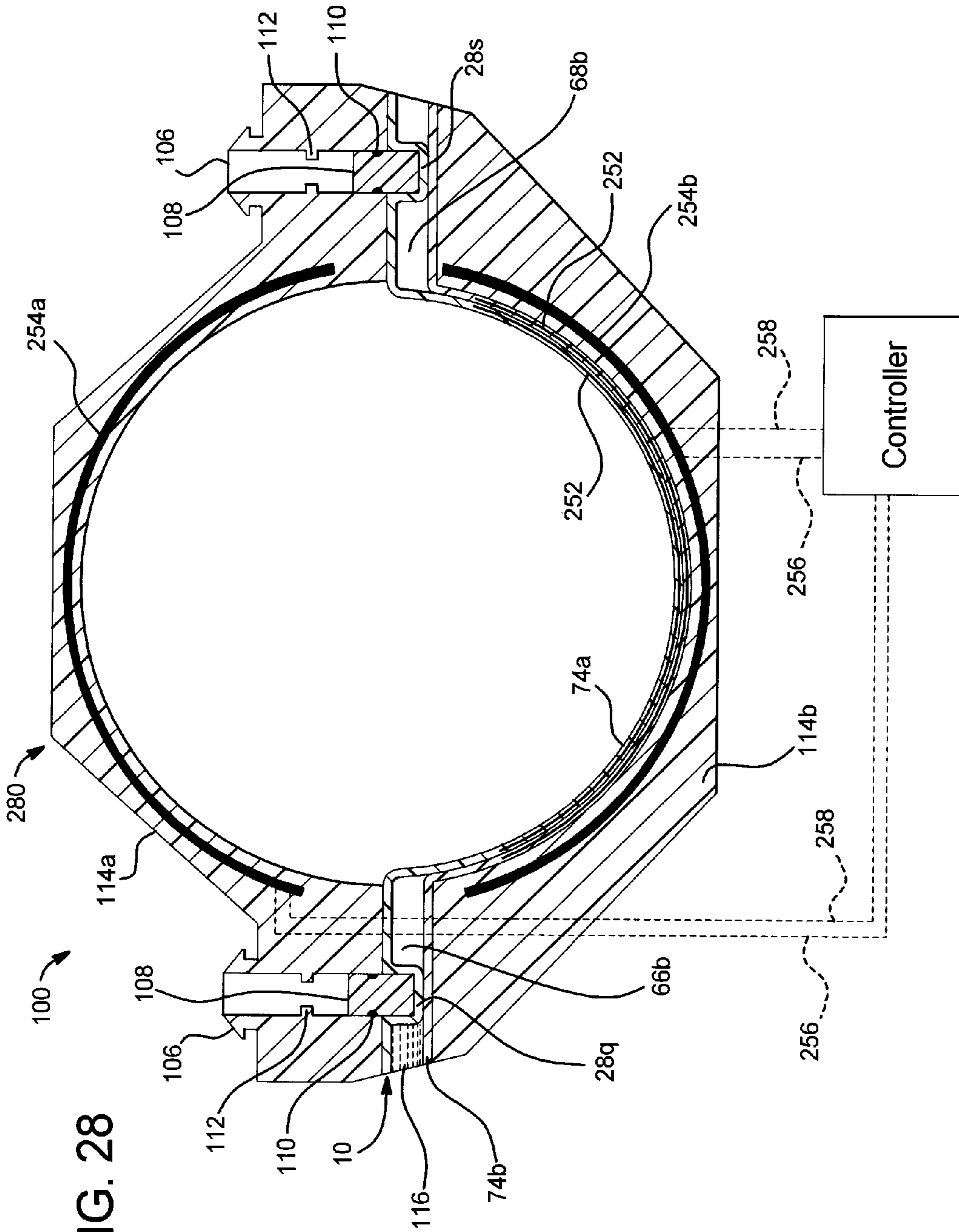


FIG. 28

1

HEMODIALYSIS SYSTEM WITH SEPARATE DIALYSATE CASSETTE

PRIORITY CLAIM

This application claims priority to and the benefit as a continuation of U.S. patent application Ser. No. 11/530,842, entitled "Medical Fluid System With Flexible Sheeting Disposable Unit", filed Sep. 11, 2006, which is a continuation-in-part of U.S. patent application Ser. No. 10/982,170, entitled "High Convection Home Hemodialysis/Hemofiltration And Sorbent System", filed Nov. 4, 2004, which claims priority to and the benefit of U.S. Provisional Patent Application No. 60/517,730, filed Nov. 5, 2003, entitled "High Convection Home Hemodialysis/Hemofiltration And Sorbent System", the entire contents of each of which are hereby incorporated by reference and relied upon.

BACKGROUND

The examples discussed below relate generally to medical fluid delivery. More particularly, the examples disclose systems, methods and apparatuses for the control of fluid flow in kidney failure treatment systems.

Due to various causes, a person's renal system can fail. Renal failure produces several physiological derangements. The balance of water, minerals and the excretion of daily metabolic load is no longer possible and toxic end products of nitrogen metabolism (urea, creatinine, uric acid, and others) can accumulate in blood and tissue.

Kidney failure and reduced kidney function have been treated with dialysis. Dialysis removes waste, toxins and excess water from the body that would otherwise have been removed by normal functioning kidneys. Dialysis treatment for replacement of kidney functions is critical to many people because the treatment is life saving.

Hemodialysis and peritoneal dialysis are two types of dialysis therapies used commonly to treat loss of kidney function. A hemodialysis ("HD") treatment utilizes the patient's blood to remove waste, toxins and excess water from the patient. The patient is connected to a hemodialysis machine and the patient's blood is pumped through the machine. Catheters are inserted into the patient's veins and arteries so that blood can flow to and from the hemodialysis machine. The blood passes through a dialyzer of the machine, which removes waste, toxins and excess water from the blood. The cleaned blood is returned to the patient. A large amount of dialysate, for example about 120 liters, is consumed to dialyze the blood during a single hemodialysis therapy. Hemodialysis treatment lasts several hours and is generally performed in a treatment center about three or four times per week.

Another form of kidney failure treatment involving blood is hemofiltration ("HF"), which is an alternative kidney failure therapy that relies on a convective transport of toxins from the patient's blood. This therapy is accomplished by adding substitution or replacement fluid to the extracorporeal circuit during treatment (typically ten to ninety liters of such fluid). That substitution fluid and the fluid accumulated by the patient in between treatments is ultrafiltered over the course of the HF treatment, providing a convective transport mechanism that is particularly beneficial in removing middle and large molecules waste products.

Hemodiafiltration ("HDF") is another blood treatment modality that combines convective and diffusive clearances. HDF uses dialysate to flow through a dialyzer, similar to standard hemodialysis, providing diffusive clearance. In

2

addition, substitution solution is provided directly to the extracorporeal circuit, providing convective clearance.

Peritoneal dialysis uses a dialysis solution, also called dialysate, which is infused into a patient's peritoneal cavity via a catheter. The dialysate contacts the peritoneal membrane of the peritoneal cavity. Waste, toxins and excess water pass from the patient's bloodstream, through the peritoneal membrane, and into the dialysate due to diffusion and osmosis, i.e., an osmotic gradient occurs across the membrane. The spent dialysate is drained from the patient, removing waste, toxins and excess water from the patient. This cycle is repeated.

There are various types of peritoneal dialysis therapies, including continuous ambulatory peritoneal dialysis ("CAPD"), automated peritoneal dialysis ("APD"), tidal flow APD and continuous flow peritoneal dialysis ("CFPD"). CAPD is a manual dialysis treatment. The patient manually connects an implanted catheter to a drain, allowing spent dialysate fluid to drain from the peritoneal cavity. The patient then connects the catheter to a bag of fresh dialysate, infusing fresh dialysate through the catheter and into the patient. The patient disconnects the catheter from the fresh dialysate bag and allows the dialysate to dwell within the peritoneal cavity, wherein the transfer of waste, toxins and excess water takes place. After a dwell period, the patient repeats the manual dialysis procedure, for example, four times per day, each treatment lasting about an hour. Manual peritoneal dialysis requires a significant amount of time and effort from the patient, leaving ample room for improvement.

Automated peritoneal dialysis ("APD") is similar to CAPD in that the dialysis treatment includes drain, fill, and dwell cycles. APD machines, however, perform the cycles automatically, typically while the patient sleeps. APD machines free patients from having to manually perform the treatment cycles and from having to transport supplies during the day. APD machines connect fluidly to an implanted catheter, to a source or bag of fresh dialysate and to a fluid drain. APD machines pump fresh dialysate from the dialysate source, through the catheter, into the patient's peritoneal cavity, and allow the dialysate to dwell within the cavity, causing the transfer of waste, toxins and excess water to take place. The source can be multiple sterile dialysate solution bags.

APD machines pump spent dialysate from the peritoneal cavity, through the catheter, to the drain. As with the manual process, several drain, fill and dwell cycles occur during APD. A "last fill" occurs at the end of CAPD and APD, which remains in the peritoneal cavity of the patient until the next treatment.

Both CAPD and APD are batch type systems that send spent dialysis fluid to a drain. Tidal flow systems are modified batch systems. With tidal flow, instead of removing all of the fluid from the patient over a longer period of time, a portion of the fluid is removed and replaced after smaller increments of time.

Continuous flow, or CFPD, systems clean or regenerate spent dialysate instead of discarding it. The systems pump fluid into and out of the patient, through a loop. Dialysate flows into the peritoneal cavity through one catheter lumen and out another catheter lumen. The fluid exiting the patient passes through a reconstitution device that removes waste from the dialysate, e.g., via a urea removal column that employs urease to enzymatically convert urea into ammonia. The ammonia is then removed from the dialysate by adsorption prior to reintroduction of the dialysate into the peritoneal cavity. Additional sensors are employed to monitor the removal of ammonia. CFPD systems are typically more complicated than batch systems.

In each of the kidney failure treatment systems discussed above, it is important to control ultrafiltration, which is the process by which water (with electrolytes) moves across a membrane, such as a dialyzer or peritoneal membrane. For example, ultrafiltration in HD is a result of transmembrane and osmotic pressure differences between blood and dialysate across a dialyzer membrane. For a given osmotic pressure, the greater the transmembrane pressure the more rapid the ultrafiltration.

Many of the above-described dialysis systems employ a pumping cassette. The pumping cassette typically includes a flexible membrane that is moved mechanically to push and pull dialysis fluid out of and into, respectively, the cassette. Certain known systems include flexible sheeting on one side of the cassette, while others include sheeting on both sides of the cassette. Positive and/or negative pressure can be used to operate the pumping cassettes.

The pumping cassettes have many design concerns. For example, one problem with the pumping cassettes is leakage. If the flexible membranes experience a pinhole or tear, fluid and air can move from one side of the membrane to the other. Movement of fluid from inside the cassette to the inner workings of the machine can damage the machine. Movement of air from the machine into the cassette can compromise the sterility of the fluid pathways defined by the cassette.

Another problem with cassette-based pumping occurs when the cassette is loaded improperly into the machine. Proper alignment is important because portions of the flexible membrane must match corresponding machine portions, e.g., pump and valve actuators. Improper loading can lead to undue mechanical stress being placed on the cassette, harming potentially the cassette and/or the actuator. Improper cassette loading can also degrade or prohibit performance of the system.

A further dilemma, especially in CFPD, is the coordination of multiple fluid deliveries. Cassette-based peritoneal pumping systems that administer fluids continuously to patients are required to withdraw fluid (ultrafiltrate) from and add fluid (concentrate) to a continuously flowing dialysis fluid loop. The additional fluids have typically necessitated additional dedicated pumps, which make the cassette and dialysis machine larger and noisier. Scheduling the operation of multiple pumps also presents a challenge to system implementers.

Yet another problem associated with cassette-based pumping is the entrapment of air or other gas in the fluid pathways. Air can enter the system via leaking connections, improper priming, faulty tubing and faulty cassettes. Patient therapy also produces various gases that enter the system. Cassette-based pumps are designed to pump fluid, not gas. Moreover, the removal and delivery of fluid from and to the patient needs to be monitored and controlled. For PD-type systems, air and gases upset volume measurement systems that assume no air or gas exists in the fluid pathways. Air and gases can also be uncomfortable for the patient and impede proper waste removal. For HD-type systems, air in the blood stream can be harmful to the patient.

Cost, ease of manufacturing, durability and reliability are additional concerns facing cassette-based dialysis systems. A need therefore exists for improved cassettes for cassette-based dialysis systems, which satisfy the above-described concerns.

SUMMARY

The examples described herein disclose dialysis systems employing a flexible pumping cassette such as: hemodialysis

(“HD”), hemofiltration (“HF”), hemodiafiltration (“HDF”), peritoneal dialysis (“PD”), including continuous ambulatory peritoneal dialysis (“CAPD”), automated peritoneal dialysis (“APD”), tidal flow APD and continuous flow peritoneal dialysis (“CFPD”) modalities). The systems may also be used in any type of continuous renal replacement therapy (“CRRT”). The examples below include a diffusion membrane or filter, such as a dialyzer, e.g., for HD or HDF, a hemofilter, e.g., for HF or the patient’s peritoneum, e.g., for PD. Moreover, each of the systems described herein may be used in clinical or home settings. For example, the systems may be employed in an in-center HD machine, which runs virtually continuously throughout the day. Alternatively, the systems may be used in a home PD machine, which is typically run at night while the patient is sleeping. One particularly suitable therapy for the embodiments described herein is home hemodialysis (“HHD”) and in particular high convection home hemodialysis (“HCHD”).

The examples below include a dialysate (replacement fluid) supply, which can be multiple bags of dialysate supply that are ganged together and used one after another. Further alternatively, each of the systems shown below can be used with an online dialysate source, such as one or more concentrate pump configured to combine one or more concentrate with water to form dialysate online. Online sources are used commonly with in-center HD systems for example. While the systems are described herein for use with dialysate, it is expressly contemplated to use the flexible sheeting cassettes and other apparatus with other medical fluids, such as saline, lactated ringers, drugs and/or blood.

Various flexible sheeting cassettes are shown and described herein. The flexible sheeting cassettes use a multitude of flexible sheets that are welded, heat sealed, adhered, chemically bonded, folded or otherwise formed together at desired places to produce fluid flow paths, fluid heating pathways, peristaltic pump paths, volumetric pumping areas, balance chambers (matched flow equalizers) and any combination thereof. The different sheets can be formed as separate sheets before attaching them together or be a single sheet that is folded one or more time to produce the different layers. The sheets provide an economical and readily producible alternative to known medical fluid pumping cassettes, which typically include a hard plastic component and one or more flexible sheet sealed to the hard plastic component.

It is expressly contemplated however to provide a cassette in which some components use a hard plastic member and others use flexible sheets only. For example, it may be advantageous to form the valves and certain pathways using a hard plastic piece in combination with one or more flexible sheet and form the pumping portion(s), balance chamber(s) and/or heating fluid pathway using flexible sheets only. Certain embodiments shown below combine flexible sheet cassettes with tubing loops, for example, tubing loops used in combination with a peristaltic pump roller. It is also expressly contemplated to provide a cassette in which the flow paths, heating pathway, pumping portion and volume control portion are each formed using flexible sheeting, but which includes a rigid frame for ease of handling, loading, etc.

In one embodiment a cassette is shown using two or three sheeting layers as needed to provide fluid pathways, a peristaltic pumping portion, a balance chamber portion, which are sealed together and formed with connectors that connect to one or more supply bag, a drain bag and a patient (as used herein, “patient” generally refers to a patient’s peritoneum, a dialyzer, a hemofilter, a extracorporeal circuit and any combination thereof). In one implementation, a separate fluid

5

heating pathway is provided and connected fluidly to the flexible sheeting cassette via separate tubes.

In another embodiment, the fluid heating pathway is formed using the same sheets that form other components of the dialysate fluid system, such as volumetric pump portions. The volumetric or membrane pumping portions pump a known volume of fluid with each stroke and therefore preclude the need for separate match flow equalizers or balance chambers.

Any of the flexible sheeting cassettes described herein can have one or more pumping portion. For example, the flexible sheeting cassettes can form multiple peristaltic pumping portions in combination with multiple balance chambers, which operate to produce an at least substantially steady flow of fresh and spent dialysate to the "patient" and drain, respectively. In another example, the flexible sheeting cassettes can form multiple volumetric or membrane pumping portions.

The flexible sheeting membranes also incorporate a vent, which can be located advantageously just down stream of an integrated or separate fluid heating pathway. This configuration enables air or gas generated via the heating to be vented or released to atmosphere. The vent for example can be located at the top of a vertically disposed or positioned cassette to allow for automatic air purging. Or, the cassette can be mounted horizontally in the machine and operate with a valve, which opens when air is detected. The System could vent/release gas/air to other parts of the disposable (such as a solution bag or drain line), not just to the atmosphere.

In an embodiment the flexible sheeting cassettes include connectors that connect the tubes that lead to fluid bags, the patient, a dialyzer, extracorporeal circuit, etc. In an embodiment the connectors include a body, which can be rigid, and which is sealed between two of the flexible sheets. One or both of the flexible sheets can have a thermoformed flow path, which is sealed to the other flexible sheet to form a closed flow path that leads from the connector body to a desired destination within the flexible sheeting cassette. An external end of the connector body can include a luered or ferruled end, which is configured to be sealed tightly to a tube running from the flexible sheeting cassette.

In an embodiment one of the flexible sheets includes a substantially circular thermoformed pathway leading to inlet and outlet pump pathways. A peristaltic pump roller or actuator operates with the substantially circular fluid pathway to form an integral peristaltic pumping portion of the flexible sheeting cassette. As discussed above, one or more such pumping portions may be provided in any single cassette. In such a case, described below are two embodiments for using a single roller to drive two different peristaltic pumping pathways. In one example, the flexible sheeting cassette is folded over a member, causing two inwardly facing peristaltic pumping portions to be coupled operably to a single peristaltic pump roller. In a second example, the peristaltic pumping pathway is a semicircle as opposed to a substantially complete circle, wherein two of the semicircular flow paths operate with the same peristaltic pump roller, to drive two different fluids through two different pathways.

Multiple embodiments for producing match flow equalizers or balance chambers using multiple flexible sheets are also disclosed herein. In one implementation, three sheets are used to create upper and lower balance chamber compartments, namely, one between an upper sheet and a middle sheet and the other compartment between the middle sheet and a lower sheet. Each compartment can have single or multiple fluid pathways leading to and from such compartment. Pumping fluid into a compartment dispenses a like amount of fluid from the other compartment and vice versa. In an embodiment,

6

each compartment includes two pathways connected thereto, wherein one pathway is an inlet pathway to the compartment and the other pathway is an outlet pathway from the compartment. In another implementation, only a single pathway communicates with each of the compartments, causing fluid entering and exiting each compartment to flow through the same single pathway.

In an alternative embodiment, two flexible sheets are formed with a rigid, e.g., spherical plastic chamber to form a balance chamber. Here, one compartment is formed between the rigid chamber and an upper flexible sheet. The second compartment is formed between the two flexible sheets. A rigid plate or backing is abutted against the lower flexible sheet, causing the upper flexible sheet to have only one direction in which to move when the lower compartment is filled. When the lower compartment is filled the upper flexible sheet is moved upwards towards an inner wall of the rigid chamber to dispense fluid from the upper compartment. Next fluid is filled into the upper compartment, pushing the upper sheet down towards the lower sheet to dispense fluid from the lower compartment.

In yet another alternative balance chamber embodiment, a plurality of flexible sheets is formed with a plurality of balance chamber tubes to form the balance chamber. The tubes act as fluid inlets and fluid outlets, which alternatively are formed via thermo-forming one or both of the flexible sheets. Again, each balance chamber compartment can include a single inlet/out tube or multiple dedicated inlet/outlet tubes to produce a single fluid inlet/outlet or separate fluid inlet/outlet.

The balance chambers are generally described herein operating with pumps, such as peristaltic pumps. In an alternative embodiment described below, the balance chamber is placed inside a magnetic field. Hence, the membrane (e.g., inner membrane) of the balance chamber that is driven back and forth within the chamber is doped or otherwise coupled with a ferromagnetic material. For example, a thin carbon layer can be sandwiched between outer flexible layers of air insert medical grade material. The magnetic field is modulated or polarized to move the impregnated membrane. A controller within the dialysis unit powers electromagnets located at either side of the balance chamber sequentially to draw the magnetic inner membrane to one side of the chamber and then the other, dispelling and drawing in fluid with each half-stroke. In this manner, the balance chamber (or dual balance chambers) is itself driven as opposed to being driven by a separate pump, eliminating the need for the second pump. As described below, the balance chamber systems sometimes use an ultrafiltration ("UF") meter, which is also typically passive or non-self driving. The UF meter can also be driven magnetically as described herein. Alternately, one of the magnetically driven balance chambers drives the UF meter. As further discussed below, volumetric pumps may also be modified to be driven magnetically.

As shown below an integrated volumetric or membrane pump can be formed using two flexible sheets and upper and lower chambers defined by the machine in which the cassette is loaded. The machine is configured to pull a vacuum on each of the separate sheets to pull the sheets toward the chamber wall and to provide positive pressure to push the sheet towards the opposing chamber wall as needed to draw in or push out fluid. A fluid-in pathway and fluid-out pathway communicate fluidly with the space between the flexible sheets.

The inlet and outlet pathways are valved to enable fluid to be pulled into the volumetric pump chamber in one step and to be pushed out the volumetric pump chamber in a second step. As shown below, to pull fluid into volumetric pump

chamber, positive pressure is removed and negative pressure is applied to the outer surface of one the flexible sheets to pull it from the other flexible sheet (which is under negative pressure from the other side of the chamber) towards its vacuum source, causing the pumping chamber between the sheets to open, create a vacuum and thereby pull fluid into the chamber. Next, positive pressure is applied to one of the sheets, pushing the flexible membranes closed and fluid out the pump outlet pathway.

Multiple embodiments are discussed herein for forming an integrated fluid heating pathway. The pathway can be a thermoformed pathway in one sheet that is bonded to a second sheet. In another embodiment, three sheets are used, wherein upper and lower pathways are formed with a flat middle sheet. In any of the embodiments described herein, the middle sheet includes one or more aperture to enable fluid, for example, to travel from an upper fluid heating pathway to a lower fluid heating pathway. Or with respect to the balance chambers, an aperture in the middle flexible membrane enables fluid exiting one (upper or lower) compartment to be combined with fluid exiting the other compartment in a single flow path.

Various embodiments are described herein for selectively forming the seals between two of three abutting sheets and for sealing three sheets to together. For example, a pattern of curable adhesive can be provided on one or more sides of the middle sheet to enable one or more outer sheets to be selectively adhered and sealed thereto. Alternatively, the energy provided by a heating die can be varied such that the heat generated by the die is set to seal only two of three sheets together or to seal all three sheets together.

As discussed above, any of the flexible sheeting cassettes can include a rigid component, which for example can include flow pathways, valve seats, rigid balance chamber portions, etc. As shown below, that rigid portion can be made to communicate with an all-flexible portion, which forms the remaining components of the cassette.

As discussed above, the peristaltic pumping portions can alternatively be tubes that are connected fluidly to a flexible sheeting cassette, which can include a heater flow path, balance chamber portion(s) and associated flow paths and valve seats.

In one embodiment one flexible sheeting cassette is provided for the dialysate portion of an HD, HF or HDF system, wherein a second blood cassette is provided. Both cassettes are loaded into the same machine in one embodiment. Alternatively, blood and dialysate portions of an HD, HF or HDF system can be formed in the same cassette.

It is therefore an advantage of the present disclosure to provide improved dialysis systems.

It is another advantage of the present disclosure to provide improved dialysis cassettes.

It is a further advantage of the present disclosure to provide improved home dialysis therapies.

It is still another advantage of the present disclosure to incorporate peristaltic pumping portions into a cassette formed from multiple flexible sheets.

It is still a further advantage of the present disclosure to incorporate membrane or volumetric pumping portions into a cassette formed from multiple flexible sheets.

It is a further advantage of the present disclosure to provide multiple ways to form fluid pathways in two or three abutting flexible membranes.

It is yet another advantage of the present disclosure to incorporate balance chamber portions into a cassette formed from multiple flexible sheets.

It is yet a further advantage of the present disclosure to provide a relatively low cost flexible sheeting cassette.

Moreover, it is an advantage of the present disclosure to provide methods for selectively sealing two of three abutting sheets or three of three abutting sheets together, for example.

Still additionally, it is an advantage of the present disclosure to provide a magnetically driven volumetric balancing or pumping device.

Additional features and advantages of the present disclosure will be apparent from, the following Detailed Description of the Invention and the figures.

BRIEF DESCRIPTION OF THE FIGURES

FIG. 1 is a schematic view of one embodiment of a cassette-based dialysis system employing a flexible sheeting cassette having a peristaltic pumping portion, a single balancing chamber volumetric control portion and an external heater bag.

FIG. 2 is a schematic view of one embodiment of a cassette-based dialysis system employing a flexible sheeting cassette having a volumetric or membrane pumping portion and an inline heating portion.

FIG. 3 is a schematic view of one embodiment of a cassette-based dialysis system employing a flexible sheeting cassette having dual peristaltic pumping portions, dual balancing chamber portions and an external heater bag.

FIG. 4 is a sectioned perspective view of Detail IV shown in FIG. 1, which highlights one embodiment of an inlet/outlet connector portion of the flexible sheeting cassettes.

FIG. 5 is a sectioned perspective view of Detail V shown in FIG. 1, which highlights one embodiment of a peristaltic portion for the flexible sheeting cassettes.

FIG. 6 is a sectioned perspective view of Detail VI shown in FIG. 1, which highlights one embodiment of a balancing chamber portion for the flexible sheeting cassettes.

FIG. 7 is a sectioned elevation view taken along line VII-VII of FIG. 6, illustrating the balancing chamber portion of the flexible sheeting cassette in operation with a dialysis machine.

FIG. 8 is a sectioned view taken along line VIII-VIII of FIG. 6, which shows upper and lower fluid pathways leading to the balancing chamber portion of the flexible sheeting cassette shown in FIG. 6.

FIGS. 9A to 9C are sectioned elevation views of Detail IX shown in FIG. 2, illustrating different valve states of a pump cycle for a volumetric pumping operating using the flexible sheeting cassettes.

FIG. 10A is a sectioned perspective view of Detail X shown in FIG. 2, which highlights one embodiment for an inline heater portion of the flexible sheeting cassettes.

FIG. 10B is a sectioned elevation view of a bi-level inline heater portion in operation with a dialysate fluid heater.

FIG. 11 is a perspective view of Detail XI shown in FIG. 2, illustrating one embodiment of an inline air vent portion for the flexible sheeting cassettes.

FIG. 12A is a sectioned elevation view illustrating one embodiment for configuring a single peristaltic pump actuator to drive fluid through two different flow paths of the flexible sheeting cassettes.

FIG. 12B is a plan view illustrating another embodiment for configuring a single peristaltic pump actuator to drive fluid through two different flow paths of the flexible sheeting cassettes.

FIG. 13 is a sectioned perspective view illustrating one embodiment of the flexible sheeting cassettes employing a pressure (or other parameter) sensing area in combination with a pressure (or other parameter) sensor.

FIG. 14 is a sectioned perspective view of the flexible sheeting cassettes showing one method and resulting apparatus for selectively sealing three flexible sheets together.

FIG. 15 is a perspective view of an example flexible sheeting cassette showing a second method and resulting apparatus for selectively sealing three flexible sheets together.

FIG. 16 is an elevation view of a portion of a flexible sheeting cassette illustrating a third method for selectively sealing three flexible sheets together.

FIG. 17 is a perspective view of one embodiment for an overall cassette which combines path forming flexible sheets with a rigid cassette portion.

FIG. 18 illustrates one embodiment for configuring a cassette having a flexible sheeting portion and a rigid portion with corresponding valve actuation, pump actuation and heater.

FIGS. 19A and 19B are sectioned elevation views showing another embodiment for a balancing chamber portion using two flexible sheets in combination with a rigid plastic domed component.

FIGS. 20A to 20D are perspective views in various stages of manufacture of a further alternative embodiment of a balance chamber portion produced via multiple flexible sheets.

FIGS. 21A to 21G are various views of one system employing a flexible sheeting dialysate cassette in combination with a separate blood-side cassette.

FIGS. 22A to 22D are perspective views of a further alternative system employing a flexible sheeting dialysate cassette in combination with a separate blood-side cassette.

FIG. 23 is a perspective view of yet another alternative medical fluid cassette for use with a system employing a gravimetric volume control methodology.

FIGS. 24A and 24B are perspective views of an alternative flexible sheeting cassette system in which the machine includes clamping members that compressively form pump, flow and fluid heating paths.

FIG. 25A is a schematic view of a fluid heating pathway formed via compressive clamping and a fluid heater operable with the compressed fluid heating pathway.

FIG. 25B is a perspective view of a separate heater bag with a fluid heating pathway formed via mechanical compression and a separate heater for the heater bag.

FIGS. 26A and 26B show a balance chamber portion of the disposable cassette formed via mechanical clamping and also illustrate a magnetic field that is used to drive the balance chamber.

FIG. 27 illustrates a balancing tube or balancing piston driven by a magnetic field.

FIG. 28 illustrates a volumetric pump driven by a magnetic field.

DETAILED DESCRIPTION

The examples described herein are applicable to any medical fluid (such as dialysate, substitution fluid and blood) therapy system requiring a disposable fluid pumping cassette. The systems are particularly well suited for the control of kidney failure therapies, such as all forms of hemodialysis (“HD”) including (“HHD”), hemofiltration (“HF”), hemodiafiltration (“HDF”), peritoneal dialysis (“PD,” including continuous ambulatory peritoneal dialysis (“CAPD”), automated peritoneal dialysis (“APD”), tidal flow APD and continuous flow peritoneal dialysis (“CFPD”) modalities). The systems may also be used in any type of continuous renal replacement therapy (“CRRT”).

The examples below include a diffusion membrane or filter, such as a dialyzer, e.g., for HD or HDF, a hemofilter, e.g.,

for HF or a peritoneum, e.g., for PD. Certain examples show a cassette with a single patient inlet and outlet, e.g., for batch type CAPD or APD. Dialysate in CAPD and APD is typically delivered to the patient, allowed to dwell for a period, and then pumped from the patient and discarded to drain. Those cycles are then repeated a number of times. The to- and from-patient lines are teed together and valved appropriately, for example, so that dialysate can be delivered and removed at different times via the same single line and connection to and from the patient.

Other systems include a dialysate inlet and a dialysate outlet, e.g., for a dialyzer or hemofilter used with HD, HDF or HF. The systems may each also be modified for use with a single or dual catheter as the case may be. CFPD typically uses a dual lumen catheter and thus requires separate inlets and outlets as well.

Moreover, each of the cassette-based systems described herein may be used in clinical or home settings. For example, the systems may be employed in an in-center HD machine, which runs virtually continuously throughout the day. Alternatively, the systems may be used in a home PD machine, which is typically run at night while the patient is sleeping. Home hemodialysis (“HHD”) (including high convection home hemodialysis (“HCHD”)) machines are also one preferred type of therapy machine for use with the embodiments described herein.

The examples below include a dialysate (or replacement fluid) supply, which for convenience is shown as multiple bags of the fluid. Alternatively, a single bag of dialysate supply is used. Further alternatively, each of the systems shown below can be used with an online dialysate or replacement fluid source, such as one or more concentrate pump configured to combine one or more concentrate with water to form dialysate online. For example, online sources are used commonly with HD systems.

Each of the systems shown herein operates with a heater that heats the dialysate or replacement fluid to a desired temperature. The heaters can be inline heaters located upstream or downstream of the fresh supply pump. The systems may alternatively operate with a batch type heater and/or a heater located upstream of the pump.

The systems also include a cassette with an inline air removal device (e.g., hydrophobic vent). Alternatively, a batch-type air removal device, such as an air trap is used. The air removal device can be located at or near the heating pathway to capture air that has egressed from the solution due to heating.

The flow schematics shown herein mainly involve the dialysate or replacement fluid portion of the kidney failure machine. HD, HF and HDF machines also include blood pumping systems. Various examples of blood cassettes are also discussed below.

HD, HF and HDF also include dialysate proportioning systems, mentioned above, which are also known and need not be described here. U.S. Pat. No. 5,247,434 (“the ‘434 Patent”), assigned to the assignee of the present application, the entire contents of which are incorporated expressly herein by reference, describes one example of a suitable proportioning system.

Referring now to the drawings and in particular to FIG. 1, one embodiment of a system employing a flexible sheeting cassette 10a is illustrated by system 10. System 100a is advantageous in one respect because it employs a peristaltic pump 30 in combination with a volumetric balancing device or balance chamber. Peristaltic pumps, such as pump 30, are typically used to pump clean or sterile fluids, such as dialysate or replacement fluid, because the pump hardware does not

contact and thus contaminate the fluid. The only part of the pump in contact with the dialysate/replacement fluid is the peristaltic pumping path or tube segments, which are sterilized before therapy. Also, because peristaltic pumps include no moving parts in contact with the dialysate/replacement fluid, the pumps are relatively inexpensive. Peristaltic pumps also lack the valves, seals and glands used in other types of pumps, which makes pump 30 for example, comparatively inexpensive and easy to maintain.

The volumetric balancing of system 100a uses first and second chambers of substantially equal volume in one embodiment. Each chamber includes two compartments, one termed a “pre-dialyzer” compartment and the other a “post-dialyzer” compartment. Each opposing “pre” and “post” compartment of a chamber is separated by a flexible diaphragm. Solenoid-actuated valves control the filling and emptying of each compartment. In general, each compartment is completely filled before its contents are discharged. Also, the “pre” compartments are alternately filled and discharged and the “post” compartments are alternately filled and discharged. Filling a “pre” compartment causes a discharge of a corresponding and opposing “post” compartment, respectively. Filling a “post” compartment causes a discharge of a corresponding and opposing “post” compartment.

Since the volumes of opposing “pre” and “post” compartments of the two chambers are equal, the system volumetrically balances the flow of dialysate to and from the dialyzer. One benefit of this volumetrically controlled system is that dialysate flow to the dialyzer can be accurately measured over a wide range of flowrates.

System 100a includes a plurality of supply bags 12a to 12c. The dialysate supply to system 100a is alternatively any of the systems described above, such as an online supply. System 100a also includes an initial drain bag 14 in the illustrated embodiment. With PD for example the patient’s peritoneum is full of spent dialysate at the beginning of therapy. That spent dialysate is from a last-fill from the previous night’s therapy. The first step in the treatment in PD is therefore to drain the spent dialysate to drain bag 14. Thereafter, supply dialysate is pumped from supply bags 12a to 12c through cassette 10a to the patient (as used herein, “patient” refers to a dialyzer, an extracorporeal circuit, a patient’s peritoneum or a combination thereof depending on the therapy involved). Those supply bags then double as drain bags over the different cycles of treatment, e.g., after the dialysate has dwelled inside the patient’s peritoneum for a designated amount of time and is thereafter pumped back through the cassette to the drain bag. For example, dialysate could be pumped initially from supply bag 12a, through cassette 10a, to the patient. After a preset dwell period, the spent dialysate is then pumped from the patient, through cassette 10a to bag 12a, which is now a drain bag. Afterwards, system 100a in a next cycle pumps fresh dialysate from supply bag 12b to the patient, and so on.

Supply bags 12a to 12c are connected fluidly to supply connectors 16a to 16c via supply tubes 18a to 18c, respectively. Supply connectors 16a to 16c are connected sealingly to flexible sheeting cassette 10a as illustrated in more detail below in connection with FIG. 4. Drain bag 14 is connected fluidly to drain connector 22 via drainline 24. Drain connector 22 is connected sealingly to flexible sheeting cassette 10a in the same manner that supply connectors 16a to 16c are connected sealingly to flexible sheeting cassette 10a as shown in more detail below in connection with FIG. 4.

Flexible sheeting cassette 10a defines or includes flow paths 26a to 26d that enable fluid flowing through lines or tubes 18a to 18c and 24 to communicate fluidly with a peristaltic pumping portion 30, which flexible sheeting cassette

10a also defines or includes. Peristaltic pumping portion 30 is shown in more detail below in connection with FIG. 5. Peristaltic pump portion 30 operates with a peristaltic pump actuator located in the dialysis machine. Each of the flow paths 26a to 26d defined by flexible sheeting cassette 10a includes or defines a valve contact portion 28a to 28d, respectively. Flow paths 26a to 26d and respective valve contact portions 28a to 28d are shown in more detail below in connection with FIG. 4.

In system 100a, fluid from one of the supply bags 12a to 12c is pumped through peristaltic pump portion 30, through a pump outlet pathway 32, through a to-heater pathway 34a, through a to-heater connector 36a, through an external to-heater tube 38a and finally to an external inline heater 40, which includes a fluid heating pathway 42a. To- and from-heater connectors 36a and 36b are sealed to flexible sheeting cassette 10a in the same manner in one embodiment as are connectors 16a to 16c and 22 shown in detail below in connection with FIG. 4.

External heater bag 40 defines a serpentine fluid heating pathway 42a, through which the fluid or dialysate travels. As the fluid or dialysate travels through the fluid heating pathway 42a, a plate, convective, radiant, inductive or other type of heater is used alone or in combination to heat the fluid. The heater heating the fluid flowing through heating pathway 42a can be located external to the dialysis machine that houses flexible sheeting cassette 10a or can be integrated into such machine. As seen in FIG. 2, a fluid heating pathway 42b is integrated alternatively into a flexible sheeting cassette 10b. One example of a fluid heating pathway is shown in more detail below in connection with FIG. 10A. FIG. 10B shows a two sided fluid heating pathway operating with a fluid heater.

Heated dialysate fluid flows from inline heater 40, through an external from-heater line or tube 38b, through a from-heater connector 36b of cassette 10a, through a from-heater pathway 34b defined by flexible sheeting cassette 10a, and to the volumetric control portion of cassette 10a, which is described in more detail below. To- and from-heating pathways 34a and 34b each define or include a valve contact portion 28e and 28f, respectively. Examples of valve contact portions are shown in more detail below by valve contact portions 28a to 28d of FIG. 4.

It should be appreciated that valve contact portions 28e and 28f are open when fluid is pumped to the patient, so that such fluid or dialysate can be heated. When fluid is pulled from the patient and pumped to drain, associated valve actuators close lines 34a and 34b at valve contact portions 28e and 28f. In the drain cycle, a valve actuator operates with valve contact portion 28g defined by or included in pump outlet pathway 32 to open pathway 32. In this manner, the heater and associated pathways and lines are bypassed during drain.

The materials used for supply bags 12a to 12c and drain bag 14 can be any suitable medical grade material, such as polyvinyl chloride (“PVC”), e.g., monolayer PVC films, non-DEHP PVC monolayer film, multilayer non-PVC films (wherein different layers are chosen to provide strength, weldability, abrasion resistance and minimal “sticktion” to other materials such as rigid cassette materials), polypropylene/polyethylene blend, polypropylene or Kraton blend, coextruded or laminated, with or without gas barrier, polyester, polyolefin, ULDPE. The materials used for external lines or tubes 18a to 18c, 24, 38a and 38b can be any suitable medical grade tubing material, such as PVC, non-DEHP PVC, polybutadiene (“PB”), ethylene vinyl acetate (“EVA”), polypropylene (“PP”) blend, polyethylene (“PE”) blend, Kra-

ton blend and polyolefin blends. The materials used for external fluid heater bag **40** including fluid pathway **42a** include PVC, PP/kraton blend.

The dialysis unit or machine (examples shown below in connection with FIGS. **21G** and **22A**) operating with flexible membrane cassette **10a** includes an apparatus configured to detect air in the dialysate flow path. One highly suitable place to detect air or other gas bubbles in the system is at a point in the flow path just downstream of fluid heater **40**. The heat from the heater causes air or other gas to egress from solution. Accordingly, an air detection sensor is positioned to operate with from-heater pathway **34b** in one embodiment. Suitable air detectors are disclosed in the parent application of the present disclosure.

Valve actuators of cassettes **10a** with valve contact portions **28h** and **28i** enable dialysate to be directed desirably and alternatively to either an inline vent **44** or to a volumetric balancing device or balancing chamber **50**. If air is detected in the system, the valve actuator operating with valve contact portion **28i** is closed, while the valve actuator operating with valve contact portion **28h** is opened, allowing the fluid to reach vent **44**, so that any air entrained in the fluid can escape from system **100a**. One embodiment for vent **44** is shown in more detail below in connection with FIG. **11**. Once the air is purged from flexible sheet **10a**, the valve actuator operating with valve contact portion **28h** is closed, while the valve actuator operating in combination with valve contact portion **28i** is opened, allowing the purged dialysate to flow to balance chamber **50**.

In an alternative embodiment cassette **10a** is mounted vertically in the machine with vent **44** located at the top of the mounted cassette, such that any air in from-heater pathway **34b** escapes automatically from vent **44**. Here, separate valve actuators and valve seats **28h** and **28i** are not needed. Further if, vent **44** is pointed upwardly, separate valve actuators and valve seats **28h** and **28i** are not needed even if cassette **10a** is mounted horizontally in the machine.

In an alternative embodiment, air in flexible sheeting cassette **10a** is pumped to heater bag **40** or to drain bag **14**. For example, air can be allowed to collect at the top of heater bag **40**, which is laid horizontally on a heater plate in one implementation. If air is detected downstream of heater bag **40**, appropriate valve seats **28** are switched so that the fluid is pumped to drain until no more air is detected.

Balance chamber **50** of the flexible sheeting cassette **10a** (and other components discussed herein) includes three plies or flexible sheets in one embodiment. One embodiment of balance chamber **50** is shown below in connection with FIGS. **6** to **8**, which will be discussed in more detail below. The three plies are sealed in a circular arrangement **52** in one embodiment to form upper and lower fluid compartments **54a** and **54b** (seen best in FIG. **7**). Fluid pumped through pump outlet pathway **32** flows eventually through balance chamber inlet pathways **56a** or **56b** as determined selectively by valve actuators operating with valve contact portions **28j** or **28k**, respectively. In the embodiment illustrated in connection with FIGS. **6** to **8**, balance chamber inlet pathway **56a** is in fluid communication with upper compartment **54a** of balance chamber **50**, while balance chamber inlet pathway **56b** is in fluid communication with lower balance chamber compartment **54b**. As described in more detail below, fluid flows from compartments **54a** and **54b**, through balance chamber outlet pathways **58a** and **58b** as determined selectively by actuators operating with valve contact portions **28l** and **28m**, respectively.

Fluid that flows through balance chamber outlet pathways **58a** or **58b** flows into a to-patient pathway **60a** as seen in FIG.

1. FIGS. **6** and **8** show one embodiment for how fluid flowing through separate balance chamber outlet pathways **58a** and **58b** eventually tees together into a single to-patient pathway **60a**.

The illustrated system **100a** of FIG. **1** can be used with APD, tidal flow PD, or CAPD, for example, which typically uses a single connection to the patient for batch-type fill and drain cycles. In such a case, to-patient pathway **60a** also serves as a from-patient pathway that communicates with connector **62a**. To perform a drain cycle, connector **62a** becomes a from-patient connector, to-patient pathway **60a** becomes a from-patient pathway, outlet pathways **58a** and **58b** to the balance chamber compartments become inlets, and the previously described inlets **56a** and **56b** at the balance chamber compartments become balance chamber outlets. The peristaltic pump operating with peristaltic pump portion **30** of cassette **10a** is run in reverse, pulling spent dialysate from the patient's peritoneum, through balance chamber **50** and associated pathways and thereafter pushing the spent dialysate to a drain bag, house drain or other appropriate drain.

It is, however, possible to use system **100a** in a hemodialysis treatment, which typically includes a dialyzer having a dialysate inlet and a dialysate outlet (not illustrated). Or system **100a** could also be used with a PD system employing a dual lumen catheter. Here, a separate from-patient pathway **60b** is teed into to-patient pathway **60a**. A separate from-patient connector **62b** is provided and placed in fluid communication with from-patient pathway **60b**. Connectors **62a** and **62b** are fixed to flexible sheeting cassette **10a** via the same apparatus and technique shown for example with connectors **16a** to **16c** and **22** in FIG. **4**. Valve actuators are configured to operate with valve contact portions **28n** and **28o** to selectively allow fluid to flow either out to-patient connector **62a** or in through from-patient connector **62b**, respectively. To pump fluid out of cassette **10a** to the patient or dialyzer, the valve actuator operating with valve contact portion **28o** is closed, while the valve actuator operating with valve contact portion **28n** is opened. To pump fluid into cassette **28a**, the valve actuator operating with valve contact portion **28n** is closed, while the valve actuator operating with contact portion **28o** is opened.

Whether a single connector **62a** is provided or dual connectors **62a** and **62b** are provided, system **100a** is configured to pump fluid to and from a dialyzer using a desired sequence of pump-to dialyzer strokes and pump-from dialyzer strokes. For example, a peristaltic pump operating with peristaltic pump portion **30** could operate in a pump-to direction to stroke balance chamber **50** ten times, each time delivering a known volume of fluid out connector **62a** to the dialyzer. Afterward, the peristaltic pump is reversed for a period of time causing for example twelve strokes of balance chamber **50** to occur, each time pulling a known amount of fluid from the dialyzer through connector **62b**, through cassette **10a**, to one of the drain bags. The additional number of strokes pulling fluid from the dialyzer constitutes an amount of ultrafiltrate removed from the patient. Alternatively balance chamber **50** is driven magnetically as described below in connection with FIGS. **26A** and **26B**.

It should be appreciated that system **100a** could also be used to perform hemofiltration. Here, to-patient connector **62a** is connected to the extracorporeal circuit directly, such that injectable quality replacement fluid can be introduced upstream or downstream (or both) of the hemofilter. The port of the hemofilter is connected to from-patient port **62b** in a dual port configuration or to single port **62a**, wherein the sequential stroke manner just described is used in either case.

In a similar matter, hemodiafiltration could be performed, wherein the line connected to to-patient connector **62a** is connected to both the extracorporeal circuit directly and an inlet of the dialyzer. Again, the outlet of the dialyzer in HDF can be connected to from-patient port **62b** or the single port **62a** depending on the configuration of cassette **10a** used.

Referring now to FIG. 2, an alternative system **100b** employs an alternative flexible sheeting cassette **10b**. System **100b** includes many of the same components that system **100a** includes. For example, system **100b** includes supply containers **12a** to **12c** and drain container **14**. As before, supply containers **12a** to **12c** are connected fluidly to cassette **10b** via supply connectors **16a** to **16c** via supply lines **18a** to **18c**, respectively. Also, drain bag **14** is connected fluidly to drain connector **22** via drainline **24**. Connectors **16a** to **16c** and **22** are each connected to flow paths **26a** to **26d**, wherein each of the flow paths has a valve contact portion **28a** to **28d**, respectively. Flow paths **26a** to **26d** all feed into a pump inlet manifold pathway **64a**.

One primary difference between system **100b** and system **100a** is that system **100b** uses volumetric or membrane pumps rather than peristaltic pumps. Here, an inlet manifold pathway **64a** communicates fluidly with pump inlet pathways **66a** and **66b**, which each lead fluidly to a respective volumetric or membrane pumping portion **70a** and **70b**. Valve actuators operating with valve contact portions **28p** and **28q** enable fluid to be pumped selectively through either volumetric pump portion **70a** or **70b** as desired. Volumetric pump portions **70a** and **70b** operate with a pneumatic and/or mechanical pump actuator located within the dialysis machine as described in more detail below in connection with FIGS. 9A to 9C. Alternatively, the volumetric pump portions are actuated magnetically as shown below in connection with FIG. 28.

In FIG. 2, pump outlet pathways **68a** and **68b** extend from the outlet side of pump portions **70a** and **70b**, respectively, and feed into a pump outlet manifold pathway **64b**. Fluid leaves the pump outlet manifold pathway **64b** then enters an alternative integral inline fluid heating pathway **42b**. Inline, integral fluid heating pathway **42b** is shown in more detail operating with a fluid heater in connection with FIG. 10A. Any air that escapes from the dialysate or other medical fluid (including blood) during heating within fluid heating pathway **42b** can be selectively removed from the system via inline vent **44**. One embodiment for vent **44** is shown in detail below in connection with FIG. 11. Air is alternatively pumped to drain or left in fluid heating pathway **42b**. Cassette **10b** can be mounted in machine vertically with vent **44** pointing upwardly to allow air to escape cassette **10b** automatically and without valve actuator and valve seat **28h** for such actuator. Further vent **44** can be pointed upwardly when cassette **10b** is loaded such that valve actuator and valve seat **28h** can be eliminated even if cassette **10b** is loaded horizontally.

If no air is detected, heated dialysate is allowed via valve actuators operating with contact portions **28i** and **28h** to be pumped to the patient (dialyzer or hemofilter, etc.) via to-patient connector **62a**. As described above in connection with system **100a**, system **100b** can alternatively include a from-patient connector **62b** (not illustrated here). In either configuration, system **100b** can perform sequential HD (including HHD), HF or HDF as described above.

In the illustrated configuration of system **100**, flexible sheeting cassette **10b** is configured to perform PD, such as CAPD, tidal flow PD and APD. Here, as described above, after dialysate has been allowed to dwell within the patient's peritoneum for a prescribed period of time, to-patient connector **62a** becomes a from-patient connector, which receives

spent dialysate from the patient. In the illustrated embodiment, spent fluid is pulled back through fluid heating pathway **42b** via pumps **70a** and **70b**, which push the spent dialysate to a suitable drain bag or drain. In an alternative embodiment (not illustrated), cassette **10b** provides a suitable bypass pathway and corresponding valve contact portions to enable returning spent fluid to bypass fluid heating pathway **42b**.

As shown, one primary difference between system **100b** and system **100a** is the incorporation of fluid heating pathway **42b** into the flexible sheeting cassette **10b**. Here, the corresponding heater is placed in the same machine housing as the pump actuator and valve actuators. As discussed above, the separate inline heater bag **40** of system **100a** can operate alternatively with a heater housed in the same unit as the pump and valve actuators of system **100a** or with a heater provided separately from the pump and valve actuator unit. It should be appreciated that the integrated, inline pathway **42b** of system **100b** can be used with the peristaltic pump portion **30** and/or balance chamber **50** of system **100a** of FIG. 1. Further, the separate heater bag **40** of system **100a** can alternatively be used with the volumetric pump portions **70a** and **70b** of FIG. 2.

As discussed, one primary difference between system **100b** and system **100a** is the use of volumetric or membrane pump portions **70a** and **70b** as opposed to the peristaltic type pump used above for system **100a**. Volumetric pump actuators operating with portions **70a** and **70b** pump a known amount or volume of dialysate with each pump stroke. The total volume pumped by volumetric or membrane pump portions **70a** and **70b** is determined by counting the number of pump strokes. The advantage here is that a separate volumetric control apparatus, such as balance chamber **50**, is not needed. Two pump actuators operate out of phase with portions **70a** and **70b** to produce an at least substantially continuous flow of dialysate to and from the patient.

All the materials described above for system **100a** are also applicable to like components of system **100b**. In operation, one of the supply valves **28a** to **28c** is opened to enable fresh dialysate to flow from one of the supply bags **12a** to **12c** into one of pump portions **70a** and **70b**, via a respective supply pathway **26a**, **26b** or **26c**. Pumped fluid flows through manifold **64a**, through inlet pathway **66a** or **66b** into pump portion **70a** or **70b**, respectively. The fluid then flows through respective outlet pathway **68a** or **68b**, through outlet manifold **64b**, through heating path **42b** where it is heated, through to-patient fluid connector **62a** into the patient.

Volumetric pump portions **70a** and **70b** can pump fluid to or from the patient using different valve sequencing. For example, to pump fluid to the patient the pump through portion **70a** and to pull fluid into pump portion **70a** the valve actuator operable with valve contact portion **28p** is opened, while the valve actuator operable with valve contact portion **28r** is closed. Next, the valves are switched to pump the volume out of portion **70a**, through heating pathway **42b** to the patient. To run in reverse, e.g., drain the patient, the above-described valve states are reversed to pull spent fluid into pump portion **70a** and then to pump the spent fluid from pump portion **70a** to a suitable drain.

Referring now to FIG. 3, a system **100c** employing a third flexible sheeting cassette **10c** is illustrated. System **100c** is similar to system **100a** of FIG. 1 and includes many of the same components, such as supply bags **12a** to **12c**, drain bag **14**, supply connectors **16a** to **16c**, drain connector **22**, and lines **18a** to **18c** connecting the supply bags to inlets connectors **16a** to **16c**, respectively. System **100c** also includes a line **24** leading from drain connector **22** to drain bag **14**. Flexible sheeting cassette **10c** includes the same valve contact portions

28a to 28h as discussed above for system 100a. System 100c operates with a separate heater bag 40 having a fluid heating pathway 42a coupled to heater lines 38a and 38b and connectors 36a and 36b. The operation of vent 44 is as described above. Air is alternatively pumped to drain bag 14 or left in heater bag 40.

One primary difference between system 100c and system 100a is that it uses two separate peristaltic pump actuators operable with separate peristaltic pumping portions 30a and 30b. The illustrated configuration for the pumping portions is upstream of the fresh and spent inlets of the dual balance chambers 50a and 50b. This configuration allows for simultaneous, two-way pumping as discussed below.

System 100c provides dual balance chambers 50a and 50b. As seen, each balance chamber 50a and 50b operates with balance chamber inlet pathways 56a and 56b and balance chamber outlet pathways 58a and 58b. Each of those pathways includes a respective valve contact portion 28j, 28k, 28l or 28m, respectively.

Simultaneous, two-way pumping requires a to-patient pathway 60a connected fluidly to a to-patient connector 62a and a from-patient pathway 60b connected fluidly to a from-patient connector 62b. From-patient pathway 60b is connected fluidly to spent pump portion 30b and to balance chamber inlet pathways 56a leading to balance chambers 50a and 50b. Thus balance chamber inlet pathways 56a are spent fluid inlets and the spent fluid is driven by a pump actuator operating with peristaltic pump portion 30b.

Fluid inlet pathways 56b on the other hand are connected fluidly to pump outlet pathway 32 leading from supply pump portion 30a. Thus balance chamber inlet pathways 56b are fresh fluid inlets receiving fresh fluid driven by a pump actuator operating with peristaltic pump portion 30a. As shown below however, balance chambers 50a and 50b operate as secondary pumps, which accept a volume of fresh or spent fluid from fresh supply pumping portion 30a or from spent supply pumping portion 30b, respectively, and expel a like amount of spent or fresh fluid, respectively.

On the outlet side of balance chambers 50a and 50b, to-patient pathway 60a is connected fluidly to outlet pathways 58b. This overall path allows fresh fluid to be delivered from the balance chambers 50 (referring collectively to balance chambers 50a and 50b) to a dialyzer, extracorporeal circuit or the patient's peritoneum depending upon the therapy being used. Outlet pathways 58a are connected fluidly to a drain pathway 26d, which is fed to drain bag 14 or one of supply bags 12 acting as a drain bag, as determined by drain valve contact portions 28d, 28u, 28v and 28w. Alternatively, drain 14 is sized to hold the volumes from each of the supply bags 12a to 12c, eliminating contact portions 28u to 28w and simplifying drain pathway 26d.

In operation, system 100c can simultaneously deliver and remove fluid to and from the patient. To do so, in one half-cycle, for example, valve actuators operating with seats 28k and 28l of balance chamber 50a and valve seats 28j and 28m of balance chamber 50b are in an open-valve state, while valve actuators operating with valve seats 28 and 28m of balance chamber 50a and valve seats 28k and 28l of balance chamber 50b are in a closed-valve state. This configuration allows pump portion 30a to deliver a volume of fresh solution through inlet pathway 56b into balance chamber 50a, which in-turn forces a previously delivered like volume of spent solution to leave balance chamber 50a, through outlet pathway 58a, drain pathway 26d, to drain 14 or one of the supply bags 12a or 12b acting as a drain bag. Simultaneously, pump portion 30b delivers a volume of spent solution through inlet pathway 56a into balance chamber 50b, which in turn forces

a previously delivered like volume of fresh solution to leave balance chambers 50b, through outlet 58b and to-patient line 60a to the patient.

Then, in a second half-cycle, valve seats 28k and 28l of balance chamber 50a and valve seats 28j and 28m of balance chamber 50b are closed, while valve seats 28j and 28m of balance chamber 50a and valve seats 28k and 28l of balance chamber 50b are opened. This configuration allows pump portion 30a to deliver a volume of fresh solution through inlet pathway 56b into balance chamber 50b, which in turn forces a previously delivered like volume of spent solution to leave balance chamber 50b, through outlet pathway 58a and drain pathway 26d, to drain or one of the supply bags 12a or 12b. Simultaneously, pump portion 30b delivers a volume of spent solution through from-patient line 60b and inlet pathway 58a into balance chamber 50a, which in turn forces a previously delivered like volume of fresh dialysate from balance chamber 50a through outlet pathway 58b, to-patient line 60a and to the patient.

As shown and described, balance chambers 50a and 50b ensure that a like volume of fresh and spent dialysate is delivered to and removed from the patient in each half-cycle. System 100c can remove excess fluid or ultrafiltrate in a number of ways. In one embodiment, both balance chambers 50a and 50b are filled with spent fluid. Next, valve contact portions 28l, 28k and 28n are opened and the pump actuator operating with pump portion 30a is run in reverse, pulling fluid from the patient through to-patient line 62a in the reverse direction. This action causes spent fluid to be pushed out drain pathway 26d to a drain via the spent fluid pulled in via pumping portion 30a. Now, both fresh compartments of balance chambers 50 are full of spent fluid and pump portion 30b causes spent fluid again to fill both spent compartments of chambers 50a and 50b with spent fluid. This causes a delivery of spent fluid from both fresh compartments of chambers 50 to the patient. A net fluid loss occurs because this volume came from the patient instead of the source. Alternatively, a valved bypass line is provided (not illustrated) leading from the to-patient line 60a to drain pathway 26d, so that the spent fluid is sent alternatively to a drain. The valved bypass line increases the UF efficiency but adds extra valves and flow paths. Either way, the above-described valve sequence is repeated as needed to remove a necessary amount of ultrafiltrate.

The above-described UF embodiments are administered intermittently. That is, they occur in some sequence with the non-UF or balanced strokes. For example, the control unit operating the pump and valve actuators could sequence system 100c to administer twelve balanced strokes and then three UF strokes. By the end of therapy, the cumulative volume of the UF strokes achieves the target UF volume, which is the volume of fluid that needs to be removed to return the patient to his or her "dry weight" as that term is known in the art.

In an alternative embodiment, system 100c provides a third peristaltic pump operating with a third UF peristaltic pumping portion (not illustrated but configured and valved at least substantially the same as pumping portions 30a and 30b) and a third UF balance chamber (not illustrated but configured and valved at least substantially the same as balance chambers 50a and 50b). In one embodiment, the inlet of the UF pumping portion tees into from-patient line 60b or connects separately to a from-patient tube extending from to the patient to from-patient connector 62b.

The outlet of the UF pump portion feeds into both compartments of the UF balance chamber. Valves are provided to allow the UF pump portion to fill a first compartment of the UF balance chamber with spent fluid, thus emptying the

second compartment of the UF balance chamber of spent fluid. Next, the second compartment is filled, emptying the first compartment of spent fluid to complete a full cycle. In each cycle a known amount of spent fluid is removed as UF. Fluid emptied from the UF balance chamber is sent via drain pathway **26d** to drain **14** or one of the supply bags **12** acting as a drain bag as described above.

The UF cycle is repeated as necessary to achieve the target UF removal volume. Importantly, this can be done while pumping portions **30a** and **30b** and balance chambers **50a** and **50b** deliver/remove a matched volume of fresh/spent fluid to/from the patient. It may be beneficial to have the ability to run the UF pumping portion and the UF balance chamber continuously, e.g., at a constant rate or at a varying rate according to a patient profile over the course of therapy. To do so, the valves controlling the UF balance chamber are switched at greater or lesser frequencies. The UF balance chamber may be sized differently, e.g., smaller than balance chambers **50a** and **50b** for finer control of UF.

The third pump operating with the UF pumping portion can be run at any desired speed relative to the pumps operating with balanced pumping portions **30a** and **30b**. FIGS. **12A** and **12B** show peristaltic pump embodiments in which a single roller drives two flexible sheeting cassette pumping portions. Given the above need for varying UF pump speed, the two pumping portions driven by the same roller (and thus at the same speed) would be matched flow portions **30a** and **30b** in one embodiment. The UF pumping portion would then operate with its own roller.

In a further alternative embodiment, the third UF balance chamber is provided but a third pumping portion is not. Here, the spent fluid pumping portion **30b** drives the UF balance chamber off of the return pathway **60b** (downstream of spent fluid pumping portion **30b**) in addition to balance chambers **50a** and **50c**. That is, the first and second compartments of the UF balance chamber are connected fluidly with the return pathway **60b** downstream of spent fluid pumping portion **30b**. The valves controlling the UF balance chamber are again switched at greater or lesser frequencies to control UF rate.

It should be appreciated that separate UF pumping portions and volumetric control devices can also be provided for systems **100a** and **100b** of FIGS. **1** and **2**. For example, a separate peristaltic pumping portion and balance chamber can be provided for system **100a** of FIG. **1**. A third volumetric UF pump can be provided for system **100b** of FIG. **2**. Such configurations allow for simultaneous balanced and UF strokes. In any of the above-described configurations, any of the balancing chambers and/or UF pumping portion can be driven alternatively magnetically as shown below in connection with FIGS. **26A**, **26B**, and **27**.

Referring now to FIG. **4**, Detail IV of FIG. **1** is shown in detail and in perspective view. FIG. **4** shows one embodiment for sealing connectors, such as supply connectors **16a** to **16c** and drain connector **22** between two plies or sheets **74a** and **74b** (which may be separate sheets or folded from the same piece of material) of flexible sheeting cassette **10a**. It should be appreciated however that the teachings of FIG. **4** apply to any of the sheeting cassettes **10** (referring collectively to flexible sheeting cassettes **10a**, **10b**, **10c**, etc.) and also to any type of connector, such as to- and from-heater connectors **36a** and **36b** and to- and from-patient connectors **62a** and **62b**.

In the illustrated embodiment, connectors **16** (referring to **16a** to **16c** collectively) and **22** each include a connector body **80**, which can be semi-rigid or rigid. Suitable materials for body **80** include semi-rigid or rigid polymers or plastics, such as, Acrylic and Cyclic Olefin Copolymer ("COC"). Body **80** includes or defines a sealing apparatus **82**, such as a luer

fitting, ferreled fitting, other type of press-fit or threaded seal. In one embodiment, supply lines **18** and drainline **24** (not shown) are removably or permanently sealed around fitting **82**. The seal can rely on press-fit alone or be aided by a medically suitable adhesive, chemical bond or weld, such as an ultra-sonic, heat or other type of weld.

In one alternative embodiment, lines **18** (referring to **18a** and **18c** of FIG. **1** collectively) and **24** fit sealingly and removably or permanently to body **80**. A permanent seal can include any of the bonding techniques discussed above, such as adhesive, heat energy, etc. In another alternative embodiment (not illustrated) one or both of first and second plies **74a** and **74b** is thermo-formed to form a male port that extends outwardly from the front edge **78a**. Supply or drain lines **18** and **24** can then seal removably or permanently around or inside the thermoformed port via any of the techniques discussed above.

As illustrated by the rows of X's (used throughout the application to illustrate a sealed seam), first ply **74a** is sealed longitudinally at seals **72a** and **72b** to second ply **74b** on either side of body **80**. Seals **72a** and **72b** can also include a seal of plies **74a** and **74b** to body **80**. As seen, seals **72a** and **72b** extend inwardly from bodies **80** to seal and form supply flow pathways **26a** to **26c** and drain pathway **26d**.

In the illustrated embodiment, pathways **26** are formed by thermo-forming a longitudinal, at least substantially semi-circular arc in one or both first and second plies or sheets **74a** and **74b**. Suitable processes for making such longitudinal arc include thermoforming and injection molding. In an alternative embodiment, the arc is not pre-formed, rather, seals **72a** and **72b** define relatively flat flow paths **26** (referring collectively to flow paths **26a** to **26d**, etc.) and the pumps are sized and configured to force fluid through the at least substantially flat plies **74a** and **74b** forming pathways **26**. Further alternatively, one or more temporary tube rod or other template instrument can be laid on sheet **74a** or **74b**. Sheet **74a** or **74b** is stretched over the tube or template and welded to sheet **74b** or **74a**, respectively. The tube or template is removed leaving pathways **26**.

A seal **72c** is made along front edge **78a** of flexible sheeting cassette **10a**. Seal **72c** includes a sheet **74a** to sheet **74b** seal in certain places and a circumferential sheet **74a/74b** to body **80** seal at connectors **16** and **22**. A seal **72d** is made along side edge **78b** of flexible sheeting cassette **10b**. Seal **72** (referring collectively to seals **72a**, **72b**, **72c**, **72d**, etc.) can be made via any one or more of the adhesive, chemical or welding embodiments discussed herein. Further, edges **78b** can be formed alternatively by folding a single piece of material at edge **78b** to form first and second sheets **74a** and **74b**. Still further, edges **78a** and **78b** can be welded to a rigid frame that provides structural support for sheeting cassettes **10a**, **10b** and **10c**. The frame aids in the handling and loading of the cassette.

In the illustrated embodiment, bodies **80** of connectors **16** and **22** are at least substantially cylindrical. In an alternative embodiment, bodies **80** are flared or tapered to provide enhanced sealing surfaces for sealing to upper and lower plies **74a** and **74b**. One configuration for tapered bodies **80** is shown and described in U.S. patent application Ser. No. 10/155,384, entitled Disposable Medical Fluid Unit Having Rigid Frame, filed May 24, 2002, owned by the assignee of the present application, the entire contents of which are incorporated herein by reference.

Valve contact portions or seals **28a** to **28d** in the illustrated embodiment are flat sections or indents formed or made at the appropriate positions along flow paths **26**. The flat sections or indents can be formed in the process of forming paths **26** or be made in paths **26** after the paths are formed. The flats or

indents tend to increase the contact area with flat headed valve actuators. It is contemplated however that valve contact portions or seals **28** do not have a different configuration from the rest of flow paths **26** and are simply areas at which the valve actuator contacts the flow paths **26**. Here, the head configuration and force of the valve actuator is sufficient to close the semi-circular or circular flow paths **26** when called upon to do so. The valve actuator can be pneumatically, mechanically, hydraulically and/or electrically actuated. For example, a fail-safe valve actuator is used in one embodiment, which is closed via a spring force and opened via a vacuum. The valve actuators are opened and closed pneumatically alternatively. Further, the valve actuators can be cams driven by a cam shaft.

Referring now to FIG. 5, Detail V of FIG. 1 is shown in more detail and in perspective view. FIG. 5 shows one embodiment for peristaltic pump portion **30** (including pump portions **30a**, **30b**, etc.). Pump portion **30** includes an at least substantially circular flow path **84**, which is formed using upper and lower plies **74a** and **74b** via any of the methods discussed herein and includes any of the configurations discussed above for fluid pathways **26**. Peristaltic pump inlet **86** and peristaltic pump outlet **88** communicate fluidly with peristaltic flow path **84** and with supply pathways **26a** to **26c** and pump output pathway **32**, respectively, shown above in connection with FIGS. 1 and 3. Inlet **86** and outlet **88** are placed in an at least substantially parallel, adjacent relationship with respect to each other in the illustrated embodiment to maximize the distance or throw of peristaltic pumping pathway **84**.

As shown, peristaltic pump portion **30** operates with a peristaltic pump actuator **90**. Peristaltic pump actuator **90** generally includes components known to those of skill in the art, such as a drive shaft **92** and at least one roller **94** driven rotatably by drive shaft **92**. One difference between the peristaltic configuration of FIG. 5 and that of known peristaltic pumps is that known pumps typically use round tubing that is looped inside of a circular race. That is, the outer circumference of the loop is abutted against the race. The drive shaft rollers contact the inner circumference of the loop and pinch the tube radially against the race. In FIG. 5, on the other hand, a race or press-plate **126** is located behind second sheet **74b**. The race or press-plate **126** is part of the dialysis machine in one embodiment and, for example, can be part of a door that is closed against flexible sheeting cassette **10a** or **10c** after it has been loaded into the machine. Rollers **94** are located within the machine on the opposing side of cassette **10a** or **10c**.

Rollers **94** spin in substantially a same plane in which sheets **74a** and **74b** reside and press pathway **84** in multiple places against plate **126** to drive fluid from inlet **86** to outlet **88**. In particular, shaft **92** spins such that rollers **94** create negative and positive pressure gradients to drive fluid from inlet **86** to outlet **88**. The thermo-formed flow paths are configured to withstand, e.g., not collapse or close, forces created by the vacuum or negative peristaltic pressures. As seen via the arrows FIG. 5, shaft **92** can be driven bi-directionally if needed as described above.

Referring now to FIG. 6, one embodiment for balance chamber **50** (referring generally to balance chambers **50a**, **50b**, etc.) used in flexible sheeting cassettes **10a** and **10c** is illustrated. FIG. 6 shows Detail VI of FIG. 1 shown in perspective view. FIGS. 7 and 8 are cross-section views of FIG. 6 taken along lines VII-VII and VIII-VIII, respectively, shown in FIG. 6. As seen in FIGS. 6 to 8, balance chamber **50** uses three plies or sheets **74a** to **74c** of flexible material. Various embodiments for sealing three separate plies together

are discussed herein. Three sheets **74a** to **74c** may be completely separate or folded twice from the same piece of material.

As seen in FIG. 6 and discussed above, balance chamber **50** includes a sealed circle **52** formed by a first seal **78e** shown by the circular axis between first sheet **74a** and second sheet **74b**. The chamber formed within the circular seal **72e** between sheets **74a** and **74b**, which form the upper balance chamber compartment **54a** as seen also in FIG. 7. A second seal **72f** is shown in phantom in FIG. 6 in which it resides beneath sheet **74a** and is made about the same sealed circle **52** between second sheet **74b** and third sheet **74c**, which form lower balance chamber compartment **54b**. In an embodiment, seals **72e** and **72f** are made at the same time or as the same seal, so that a single sealing process, e.g., a welding or chemical bonding process, forms both seals **72e** and **72f** simultaneously and associated comparatively. It is contemplated, however, to form one of seals **72e** and **72f** first and thereafter form the second of the two seals **72e** and **72f**. Seals **72e** and **72f** can be made via any of the methods described herein. Additional seals (not illustrated) are made along the edges of the three sheets **74a** to **74c** and elsewhere in cassette **10a** or **10c** as discussed herein.

In the illustrated embodiment seal **72e** extends to form balance chamber inlet **56a** and balance chamber outlet **58a**. Enough of balance chamber outlet **58a** is seen such that valve contact portion or seat **28l** shown in FIG. 1 is also seen in FIGS. 6 and 7. Seal **72f** also extends to form balance chamber inlet **56b** and balance chamber outlet **58b**. Enough of balance chamber outlet **58b** is illustrated so that valve seat **28m** is shown in hidden and in phantom in FIG. 6 and is also seen in FIG. 8. As seen in FIG. 1, balance chamber outlet pathways **58a** and **58b** combine into two patient pathway **60a**. FIGS. 6 and 8 illustrate one embodiment for enabling fluid to travel between two flexible sheeting pairs or levels. As seen, middle flexible sheet **74b** defines an aperture or opening **96**, which is located directly above the distal end of balance chamber outlet **58b** and is inline with balance chamber outlet **58a** and the subsequent to-patient pathway **60a**. In this configuration, fluid exiting lower balance chamber compartment **54b** travels through balance chamber outlet **58b**, upwardly through second sheet **74b** via aperture **96**, into balance chamber outlet **58b** and to patient pathway **60a**, which are located and defined by flexible sheets **74a** and **74b**.

FIG. 8 illustrates a cross section of sealed plies **74a** to **74c** from a front view as cassette **10a** is sectioned through pathways **58a** and **58b** shown in FIG. 6. As seen, in FIG. 8 valve seat **28m** is located laterally offset from valve seat **28l**, so that cooperating valve actuators can open and close pathways **58a** and **58b** independently. That is, a valve actuator can close either valve seat **28l** or **28m** without also closing either of flow path **58b** or **58a**, respectively. FIG. 8 also shows aperture **96** in cross section, which is formed in sheet **74b** and which enables fluid communication between paths **58a** and **58b**, so that flow from upper and lower compartments **54a** and **54b** can be combined into to patient pathway **60a**. FIG. 8 further shows that pathways **58a** and **58b** can be raised via thermoforming or other method to provide a gap between the inner surface of plies **74a** and **74c** and the outer surfaces of ply **74b**.

Referring now to FIG. 7, one apparatus and method for operating balance chamber **50** (referring generally to each of the balance chambers described herein) is illustrated. Balance chamber **50** is shown in operation with a portion of the dialysis machine **100a** and **100c** (operating with cassettes **10a** and **10c**, respectively). Dialysis machine **100a** or **100c** includes or defines first and second chamber forming members **102a** and **102b**. For example, one of members of **102a** or **102b** is

stationary and configured to accept a flexible sheeting cassette, such as cassette **10a** or **10c**. The other of chamber forming members **102a** or **102b** is part of a door that is closed onto the opposing side of flexible sheeting cassette **10a** and **10c** after it has been loaded into dialysis machine **100a** or **100c**.

Chamber forming members **102a** and **102b** each define or include a port **104** to which a tube (not illustrated) is releasably or permanently secured via any of the methods and embodiments discussed above in connection with connectors **16** and **22** of FIG. 4. In an embodiment, after cassette **10a** or **10c** is loaded into machine **100a** or **100c**, a negative pressure or vacuum is drawn on ports **104**, pulling first and third plies or sheets **74a** and **74c** against the inner at least substantially spherically shaped cavities defined by first and second members **102a** and **102b**. Although members **102a** and **102b** are shown defining at least substantially spherical shapes, other suitable cross-sectional shapes may be used, such as substantially triangular or substantially trapezoidal shapes. Further, although not illustrated, members **102a** and **102b** can define air channels that extend radially from ports **104** in various directions to help spread the vacuum across a larger surface of plies **74a** and **74c**. Such channels are shown and described in U.S. Pat. No. 6,814,547, entitled Medical Fluid Pump, assigned to the assignee of the present application. Once sheets **74a** and **74c** are pulled via vacuum against the inner surface of chamber forming members **102a** and **102b**, respectively, balance chamber **50** is ready for operation. In an alternative embodiment, negative pressure is not applied against sheets **74a** and **74c** and thus ports **104** are not needed. Here, the positive pressure of the dialysate or fluid is enough to spread, respectively, sheets **74a** and **74c** against members **102a** and **102b**, respectively, and to drive middle sheet **74b** between sheets **74a** and **74c**.

FIG. 7 illustrates a state of operation in which no fluid has been delivered to balance chamber **50**. Accordingly, middle or driving sheet **74b** is not pushed towards either upper sheet **74a** or lower sheet **74c**. Section VII-VII taken through the detail of FIG. 6, for FIG. 7 includes valve seat **23l**. As seen in FIG. 8, valve seat **28m** is not aligned with valve seat **28l** with respect to the section plane along line VII-VII of FIG. 6. Accordingly, valve seat **28m** is not seen in the sectioned view of FIG. 7 because that view valve seat **28m** in that view resides in front of valve seat **28l**. Valve seat **28l** is shown operating with a valve actuator **106**, which is part of machine **100a** or **100c**. For simplicity, valve actuator **106** is shown as an entirely pneumatically operated valve actuator. Here, positive air pressure is applied to the port of actuator **106** to force a plunger **108** to compress valve seat **28l** against second sheet **74b** to close balance chamber outlet **58a**. Actuator **106** includes an o-ring seal **110**, which creates a sliding seal between plunger **108** in the inner, e.g., cylindrical housing of valve actuator **106**. To open balance chamber outlet **58a**, a negative pressure is applied to port **106**, pulling plunger **108** upwards against stop **112**, enabling fluid to open seat **28l** and flow outwardly from upper balance chamber compartment **54a** through balance chamber outlet **58a**. FIGS. 6 to 8 do not show valve seats **28j**, **28k** or **28l** which communicate with valve actuators, such as valve actuator **106**. These actuators and seats control the inlet of balance chamber **50a** and the inlet and outlet of balance chamber **50b** of FIG. 1.

In operation, to fill upper balance chamber compartment **54a**, plunger **108** is pressurized and closes valve seat **28l** and balance chamber outlet **58a**. The valve actuator **106** operating with balance chamber inlet **56a** is opened, enabling fluid to fill upper balance chamber compartment **54a**. If fluid has already filled lower compartment **54b**, the fluid entering com-

partment **54a** pushes the fluid from lower balance chamber compartment **54b**, through balance chamber outlet **58b** to its destination. To do so, a valve actuator **106** operating with balance chamber outlet **58b** is opened, while a valve actuator **106** operating with inlet **56b** is closed. Because the volume defined by compartments **54a** and **54b** is fixed and because second sheet **74b** is pushed all the way against sheets **74a** or **74c** in each half stroke, the same volume of fluid is outputted through balance chamber outlets **58a** and **58b** in each half stroke. Accordingly, flexible sheets **74a** and **74c** are made of a suitably stretchable, compliant and leak-free material such as one of those materials listed above for sheets **74** (referring collectively to sheets **74a** to **74c**). As discussed below in connection with FIGS. 26A and 26B, sheet **74b** is made alternatively to be magnetic and driven alternatively magnetically.

Referring now to FIGS. 9A to 9C one apparatus and method of operating volumetric pumps **70** is illustrated. The portion of cassette **10b** shown in FIG. 2 and marked as Detail IX is shown in front, cross-sectioned view in FIGS. 9A to 9C, which shows volumetric pump **70b**. The teachings with respect to **70b** are applicable to volumetric pump **70a**.

Volumetric pump **70b** is shown operating with a dialysis machine **100b**, which uses cassette **10b**. Machine **100b** includes first and second pump chamber forming members **114a** and **114b**, which define the shape of the volumetric pump **70b**. Cassette **10b** is configured to be loaded within the machine **100b** such that a circular flexible membrane portion of cassette **10b** as seen in FIG. 2 is in alignment with the spherically shaped chamber defined by pump chamber forming members **114a** and **114b**. Also, valve seats **28q** and **28s** are aligned with valve actuators **106** shown in FIGS. 9A to 9C. Valve actuators **106** operate as described above in connection with FIG. 7 and include a plunger **108**, which slides back and forth within the actuator body.

Chamber **70b** uses first and second flexible sheets **74a** and **74b**. First and second pump chamber forming members **114a** and **114b** each include a port **104** described above in connection with FIG. 7. As discussed below, negative and positive pressure are used to drain sheets **74a** and **74b**. Alternatively, one of sheets **74a** or **74b** can be driven mechanically. A suitable hybrid mechanical/pneumatic pump is shown and described in U.S. Pat. No. 6,819,547 listed above. Although the spherical shape shown in FIGS. 9a to 9c is one suitable shape, other shapes could be defined for volumetric pump **70**, such as a trapezoidal or triangular shape.

FIG. 9A shows an initial state for volumetric pump **70b**. Here, negative pressure is applied to port **104** of chamber forming member **114b**, which pulls second flexible sheet **74b** to conform with the inner surface of second chamber forming member **114b**. At the same time, positive pressure is applied to port **104** of first pump chamber forming member **114a**. The positive pressure causes first flexible sheet **74a** to be pressed against second flexible sheet **74b**. In FIG. 9A, a positive pressure is applied to both valve actuators **106**, closing valve seats **28q** and **28s**. Again, valve actuators **106** can be any combination of pneumatic, mechanical and/or electrically operated. As further seen in FIG. 9A, dialysate or medical fluid (including blood) **116** is pressurized against valve seat **28q**, but is precluded from entering into the sealed chamber of volumetric pump **70b**.

In FIG. 9B, the negative pressure at port **104** of lower pump chamber forming member **114b** is maintained as is the positive pressure applied to valve actuator **106** at valve seat **28s**. A negative pressure is applied to valve actuator **106** at valve seat **28q**, which pulls and holds plunger **108** to and against stop **112**, allowing fluid **116** to flow through pump inlet pathway

66*b* and into the chamber of volumetric pump 70*b*. The force of fluid 116, e.g., via gravity may be enough to cause first flexible member 74*a* to be pushed against inner surface of upper pump chamber forming member 114*a*. Alternatively, a negative pressure can be applied at port 104 of member 114*a* to pull first flexible sheet 74*a* against the inner surface of the member. This action causes a vacuum, which pulls fluid 116 into the pump chamber. As with the peristaltic pump, the thermo-formed flow paths are configured to withstand, e.g., not collapse, under the negative pressure of the membrane pumping. In either case, fluid 116 fills the at least substantially spherical cavity between sheets 74*a* and 74*b* and stops against valve seat 28*s*, which is still in its closed position.

In FIG. 9C, valve seat 28*q* is closed, while valve seat 28*s* is opened. Negative pressure is maintained at lower port 104, so that sheet 74*b* is pulled against member 114*b*. Here, a positive pressure is applied to port 104, closing first flexible sheet 74*a* against second flexible sheet 74*b*, causing fluid 116 to be pushed out of the at least substantially spherical chamber of volumetric pump 70*b*, through pump outlet pathway 68*b*, to its desired destination. First and second membranes 74*a* and 74*b* are now at the position showed in FIG. 9A, so that pump 70*b* is able to repeat the above described cycle as soon as valve seat 28*s* is closed. As shown below in connection with FIG. 28, membranes 74*a* and 74*b* are made alternatively to be magnetic and driven alternatively magnetically.

The pump out and fill strokes of pumps 70*a* and 70*b* in FIG. 2 can be staggered such that the flow of dialysate or medical fluid (including blood) through cassette 10*b* is at least substantially continuous. Because the volume formed by the chamber of members 114*a* and 114*b* is known and because first flexible sheet 74*a* is moved repeatedly to the upper and lower surfaces of the chambers, the volume of fluid pumped with each stroke is known and repeatable. Accordingly, a separate volumetric control apparatus, such as balance chamber 50, is not needed. The total volume of fluid pumped is equal to the volume of each stroke multiplied by the number of strokes. UF is controlled via one of the methods discussed above.

The volumetrically controlled chambers of balance chamber 50 and volumetric pumps 70 are formed in an embodiment via the respective circular seals. In an alternative embodiment, the respective seals are made larger in diameter than needed to achieve the desired volume. Here, a seal between the sheets 74 is created by the pressure of the door pressing against the machine, or a first machine part pressing against a second machine. As shown and discussed in connection with FIGS. 24A and 24B, the machine seal is sized to form the proper diameter sphere to achieve the desired volume. The mechanical clamping seal lessens alignment constraints. The machine to machine seal can be secured manually, e.g., via a lever or lock, clamps, cam-action press-fit, etc. or secured additionally or alternatively formed with the help of pneumatic or electromechanical pressure. FIGS. 25A and 25B discussed below show embodiments for fluid heating pathways formed via mechanical clamping and a heater operable with such fluid heating pathway. FIGS. 26A, 26B and 28 discussed below show embodiments of balance chamber and volumetric pump portions of the flexible sheeting cassette, respectively, formed via mechanical clamping and one embodiment for driving the membranes within the balance and pump chambers.

Referring now to FIGS. 10A and 10B, two different embodiments for an integrated heater path for the flexible sheeting cassettes discussed herein are illustrated. FIG. 10A illustrates Detail X of flexible sheeting cassette 10*b* shown in FIG. 2. FIG. 10B shows an alternative three-layer, dual-sided

heater path portion. FIG. 10A shows heater or heater plates 118, while FIG. 10B shows dual heaters or heater plates 118*a* and 118*b*. Heaters or heater plates 118 (referring collectively to heater 118 of FIG. 10A and heater plates 118*a* and 118*b* of FIG. 10B) can perform any suitable mode of heat transfer, such as electric resistance, inductive, radiant, convective and any combination thereof. As shown in FIG. 10A, heater 118 is continuous beneath fluid heating pathway 42*b*. In FIG. 10B, heater elements 118*a* and 118*b* are localized around the fluid pathways 42*c* and 42*d* of the flexible sheeting cassette.

In FIG. 10A, fluid heating pathway 42*b* is made of first and second sheets 74*a* and 74*b*. A semi-circular or other suitable cross-sectional shaped serpentine pathway is formed in sheet 74*a* via any of the apparatuses and methods discussed above in connection with FIG. 4. Alternatively, both sheets 74*a* and 74*b* can form semi-circular halves, which together form a circular whole. If so, heater 118 can be formed or tailored with a semi-circular indented heating pathway to increase surface contact. A continuous outer seal 72*g* is made around the outside of the loops or serpentine twists of fluid heating pathway 42*b*. A continuous inner seal 72*h* is made along the inner curve of pathway 42*b*. Seals 72*g* and 72*h* are made via any of the methods discussed above. Edge seal 72*i* is also made along edge 78*c* as seen in FIG. 10A. Alternatively, edge 78*c* is made via a fold. In operation, dialysate or fluid flows through pathway 42*b* and is heated via heat energy from heater 118.

In FIG. 10A, flexible sheeting cassette 10*b* is loaded on top of or is abutted vertically against heater 118. In FIG. 10B, the flexible sheeting cassette is loaded between two insulative housings 120*a* and 120*b*. Heater elements 118*a* are fixed within insulative heater housing 120*a*. Heater elements 118*b* are likewise fixed in insulative heater housing 120*b*. Housings 120*a* and 120*b* may be part of the dialysis machine or part of a separate heater.

The fluid heating pathways 42*b* and 42*c* of FIG. 10B are formed from three sheets 74*a*, 74*b* and 74*c*. Second sheet 74*b* serves as a backing to the thermally formed pathways 42*c* and 42*d* in sheets 74*a* to 74*c*. Sheets 74*a* and 74*c* are sealed at once or at different times to middle sheet 74*b* via any of the sealing methods discussed above. As seen additionally in FIG. 10B, apertures 96 are made in second sheet 74*b* to enable dialysate to flow from the lower fluid heating pathway 42*d* of third sheet 74*c* into the upper fluid heating pathway 42*c* of sheet 74*a* or vice versa. FIG. 10B therefore provides an efficient fluid heating apparatus, which in essence doubles the heating capacity for the same surface area versus the flexible sheeting cassette shown in FIG. 10A. Dual pathways such as the pathway 42*d* could also be made with a separate heater bag 40 of FIGS. 1 and 3.

Referring now to FIG. 11, one embodiment for mounting vent 44 into one of the flexible sheeting cassettes 10 (referring collectively to flexible sheeting cassettes 10*a* to 10*c*) is illustrated. In particular, FIG. 11 shows Detail XI of flexible sheeting cassettes 10*b* of FIG. 11. Flexible sheeting cassette 10*b* includes first and second flexible sheets 74*a* and 74*b*. Those sheets are sealed around vent 44, which includes a vent body 46 and a filter 48. Filter 48 in one embodiment is a hydrophobic membrane or other type of filter that allows air but not fluid or dialysate to pass through such filter. Vent 44 is fixed to sheets 74*a* and 74*b* in much the same manner as connectors 16 and 22 of FIG. 4. To that end, seals 72*a* and 72*b* are made on either side of body 46 of filter 48 and/or to body 46 itself. Seals 72*a* and 72*b* extend to form a fluid pathway, which can be aided by a thermo-formed shape created or in one or both of sheets 74*a* and 74*b*.

In operation, if air is detected in heated dialysate, a valve seat **28h** as shown in FIGS. **1** to **3** is opened, allowing the fluid to reach vent **44** and push the air through vent **48**. Afterwards, the fluid is pumped to its desired destination. Alternatively, as described above, vent **44** is pointed vertically when its associated cassette is mounted, so that a separate valve actuator and seat are not needed.

Referring now to FIG. **12A**, one embodiment for driving fluid through two flow paths using a single peristaltic pump actuator **90** is illustrated. Actuator **90** includes a drive shaft **92** and rollers **94** described above in connection with FIG. **5**. Flexible sheeting cassette, e.g., two pump cassette **10c**, when loaded, is slid horizontally or vertically over a shaft **122**, such that a slot **124** in sheets **74a** and **74b** slides over a shaft **98** of peristaltic pump actuator **90**. Rollers **94** drive fluid through both pumping portions **30a** and **30b** shown for example in cassette **10c** of FIG. **3**. Cassette **10c** is mounted such that second sheet **74b** is abutted against race plates **126a** and **126b**, which provide a rigid surface against which the flow paths of pumping portions **30a** and **30b** can be compressed by rollers **94**, similar to press-plate **126** of FIG. **5**. In the illustrated embodiment, rollers **94** drive fluid in the same direction into and out of pumping portions **30a** and **30b**. As discussed above, one use for the configuration of FIG. **12** is to provide a single peristaltic pump actuator **90** that drives two pumping portions **30a** and **30b**, which in turn feed the inlets of balance chambers **50a** and **50b** with fresh or spent fluid.

Referring now to FIG. **12B**, a second embodiment for using a single peristaltic pump actuator **90** to drive fluid through two pumping flow paths is illustrated. Here, peristaltic pumping portions **30a** and **30b** are configured as semi-circles or half-circles. Shaft **92** spins rollers **94** (actuator **90** can have any suitable number of rollers **94**) through a full 260 degrees to drive fluid through both fluid pathways of pumping portions **30a** and **30b**. A suitable race plate (not illustrated), such as race plate **126** of FIG. **5**, is mounted behind flexible sheeting cassette **10b** to provide a rigid surface against which rollers **94** can compress the raised pathways **84a** and **84b** of pumping portions **30a** and **30b**. Unlike the dual pumping embodiment of FIG. **12A**, the dual pumping embodiment of FIG. **12B** drives fluid in opposite directions as seen by oppositely disposed inlets **86a/86b** and outlets **88a/88b**. In both the embodiments of FIGS. **12A** and **12B**, however, shaft **92** can spin in either of two directions as shown by the arrows in FIG. **12B**.

Dialysis machine **100** (referring collectively to each of the machines **100a**, **100b**, etc.) uses many different sensors, such as pressure sensors, flow sensors, temperature sensors, air bubble detectors, solution identification detectors to check for example for peritonitis, composition and pH, conductivity sensors and ultrasound sensors, e.g., for air or blood detection. Those sensors are used typically to sense some parameter of the dialysate or fluid being pumped through one of the flexible sheeting cassettes **10**.

Referring now to FIG. **13**, one embodiment for operating a sensor **130** with any one of the flexible sheeting cassettes **10a** to **10c** is illustrated. Sensor **130** can be any of the above-described types of sensors and includes leads or wires **132** that lead to a control unit or controller of dialysis machine **100**. Sensor **130** senses a parameter of dialysate or medical fluid (including blood) flowing through a flow path **128**. Cassette **10** (any cassette herein) is mounted such that a sensing area **134** is aligned with sensor **130**. Sensing area **134** is an expanded flow path area defined by seals **72a** and **72b**, which slows down the flow of fluid, and can increase sensing time and accuracy. Seals **72a** and **72b** are made via any of the methods and embodiments discussed above. Sensing area **134** is shaped and sized to conform to the head of sensor **130**.

Referring now to FIG. **14**, one embodiment for making different seals between three sheets **74** of material is illustrated. In FIG. **14**, sheets **74b** and **74c** are illustrated. Sheet **74a** (not illustrated) is sealed to the top of sheet **74b**. A flow path **128** is made between sheets **74b** and **74c**. As illustrated, a thermo-formed indent or raised portion is made in sheet **74c**, which is then sealed to sheet **74b** via any of the different methods discussed above for seals **72a** and **72b**. Next, a printable adhesive is deposited on the upper surface of sheet **74b** along seal lines **72j** and **72k**. One suitable printable adhesive is cyclohexanone, e.g., for polyvinyl chloride ("PVC") sheeting, or a polyester elastomer for other types of sheeting. Next, sheet or ply **74a** is placed as desired onto the top of sheet **74b**. Radio frequency ("RF"), ultraviolet ("UV") energy or heat is then applied to adhesive seal lines **72j** and **72k** to activate the printed adhesive along the applied pattern, sealing sheet **74a** to **74b**. In this manner, the three sheets **72a** to **72c** can form any desired seal pattern (same or different) between sheets **74a** and **74b** and between sheets **74b** and **74c**.

Referring now to FIG. **15**, another method for selectively sealing three sheets **74a** to **74c** of flexible material to form a flexible sheeting cassette is illustrated. A sealed seam **136** extends along one length of the cassette **10d**, for example at or near the middle of the other length of the cassette. Seam **136** enables the cassette to be maneuvered and folded to make selectable seams in the three different sheets **74a** to **74c**. This method applies to any flexible sheeting cassettes discussed above. For purposes of illustration, flexible sheeting cassette **10d** of FIG. **15** includes the single peristaltic pump **30** and balance chamber **50** of FIG. **1** with an incorporated fluid heating pathway **42b** of FIG. **2**. As shown above, many features of the flexible sheeting cassette require only two sheets **74a** and **74b**. Other components such as balance chamber **50** require three sheets **74a** to **74c**. It is therefore contemplated to provide a cassette **10d**, which includes three sheets or plies **74** in areas requiring three sheets and only two sheets **74a** and **74b** in other areas of cassette **10d** requiring only two sheets. In cassette **10d**, three sheets **74a** to **74c** are used alternatively over the whole cassette **10d**. Again, sheets **74a** to **74c** can be separate or formed by folding a single piece of material one or more times.

The left side of cassette **10d** is used to make the three layer dual sided heating flow paths **42c** and **42d** discussed above in connection with FIG. **10B**. As illustrated, one of the outwardly facing flow paths, such as flow path **42d** is formed first by sealing sheets **74b** and **74c** together. Next, sheet **74a** is sealed to the combination of sheets **74b** and **74c**. In an embodiment, sheet **74a** is sealed to the combination of sheets **74b** and **74c** via the printable adhesive described above. In another embodiment, enough energy is applied to the outside of sheet **74a** and **74c** to chemically bond or melt sheets **74a** and **74b** together. Further alternatively, sheets **74a** to **74c** can be secured to form fluid heating pathways **42c** and **42d** simultaneously. Middle sheet **74b** defines apertures **96** as discussed above that reside between fluid heating pathways **42c** and **42d**.

The right side of cassette **10d** is used to form balance chamber **50**, peristaltic pump **30**, pressure sensing area **134**, fluid flow pathways **26a** to **26d** and other flow paths associated with the above-listed components. Here, flexible sheets **74a** and **74b** are sealed together first, after which sheet **74c** is sealed to sheet **74b**, e.g., to complete balance chamber **50**. Although not illustrated, additional flow paths can be formed between sheets **74b** and **74c**, with one or more apertures **96** allowing fluid to flow from flow paths or flow apparatuses formed via sheet **74a** and **74b** and ones formed between sheets **74b** and **74c**. Sheet **74c** can be sealed to sheet **74b** via

the printable adhesive or alternatively or additionally by applying energy through all three sheets 74a to 74c.

As illustrated, pump output pathway 32 extends from peristaltic pumping portion 30 across seam 136, through mating apertures defined in sheets 74a and 74b, into the lower fluid heating pathway 42d, through its serpentine path, back through another set of mating apertures in sheets 74a and 74b, into and through upper fluid heating pathway 42c, before extending into balance chamber 50 and out to patient connector 62a.

Referring now to FIG. 16, another method for sealing three sheets 74a to 74c together is illustrated. In FIG. 16, layers 74a to 74c are sealed using die sealing apparatuses 136a and 136b using machinery built for example by KIEFEL Extrusion GmbH, Cornelius-Heyl-Str.49, 67547 Worms/Germany. Apparatuses 136a and 136b apply heat to sheets 74a to 74c in a predefined die pattern. The die pattern includes areas in which all three sheets 74a to 74c are sealed together and other areas in which only two of sheets 74a and 74b or 74b and 74c are sealed together.

In a conductive die sealing machine, each die apparatus 136a and 136b is controlled to output a desired amount of heat in direct contact with outer sheets 74a and 74c. For example, die apparatus 136a can be set to output more heat than die apparatus 136b. Using this conductive type of heating, if it is desired to seal middle layer 74b only to sheet 74a or 74c, apparatus 136a or 136b on the non-sealing side of either sheet 74a or sheet 74b is set to deliver a lesser amount of heat to prevent sealing between that sheet and middle sheet 74b. The heat of the opposing die apparatus 136a or 136b contacting the sheet 74a or 74c that is to form a seal with sheet 74b is set to output a higher amount of heat, enough to melt the two sheets and seal the sheets in a desired pattern. The temperatures of hot and cold die apparatuses 136a and 136b are set to create a temperature profile that is higher than the melting temperature of middle layer 136b on the side to be sealed and lower on the opposing side of sheet 136b to prevent this side of the middle layer from melting. To this end, it may be that one of die apparatuses is de-energized completely. The die machine is accordingly capable of controlling the heat outputs of each apparatus 136a and 136b independently to heat the different sheets 74a to 74c to the desired temperatures.

In another embodiment, the die sealing machine is of a radio frequency ("RF") type. Here, one of the apparatuses 136a and 136b is positive and the other is negative and direct or indirect contact with sheets 74a and 74c. RF-type sealing is especially well-suited for sealing PVC, e.g., PVC tubing and PVC sheeting, although it can be used to seal other kinds of tubing and sheeting materials listed herein. RF-type sealing can be used in the embodiment of FIG. 15, for example, to seal the three sheets in multiple steps.

Referring now to FIGS. 17, 18, 19A and 19B, in an alternative embodiment, a cassette 10e includes a flexible portion 138 and a rigid portion 140. Flexible portion 138 includes first sheet 74a and second sheet 74b. Peristaltic pumping portion 30 and inline fluid heating pathway 42b are formed via sheets 74a and 74b in flexible portion 138 in any manner described above. With cassette 10e, however, balance chamber 50 is formed using two sheets 74a and 74b instead of the three sheet version described above. Here, balance chamber 50 is formed partially via a rigid chamber 142 formed in rigid portion 140. As seen in FIG. 18, flexible portion 138 is folded under or otherwise attached to the underside of rigid portion 140. When this occurs, the flexible membrane portion of balance chamber 50 aligns with and is thereafter sealed to rigid chamber 142 of rigid portion 140.

FIG. 18 also shows heater 118 operating with heating pathway 42b and peristaltic pump actuator 90 operating with peristaltic pumping portion 30. Valve actuators, such as actuators 106 discussed above, are provided in valve actuation unit 144. Valve actuation unit 144 resides on the opposing side of cassette 10e from heater 118 and pump actuator 90. In the illustrated embodiment valve actuation unit 144 can be part of a door that presses valve actuators 106, heater 118 and pump actuator 90 in place against the appropriate positions of cassette 10e.

Valve seats, such as seats 28a to 28d, are provided as part of rigid portion 140 of cassette 10e. Rigid flow paths, such as flow paths 26a to 26d, 32, 58a and 58b, communicate with pumping portion 30, balance chamber 50, their associated flow paths and fluid heating pathway 42b of flexible portion 138 via apertures, such as apertures 96 provided in one or more sheets 74b and 74a with the rigid fluid pathways.

Regarding balance chamber 50, flow paths 56a and 58a flow from the flexible portion of balance chamber 50 of flexible portion 138 to rigid pathways defined by rigid portion 140. Valve seats 28j to 28m are located in rigid portion 140. Further, pathways 56b and 58b leading to rigid chamber 142 are also provided in rigid portion 140.

Referring now to FIGS. 19A and 19B, a balance chamber 50 constructed from rigid chamber 142 of rigid portion 140 and two flexible sheets 74a and 74b of flexible portion 138 of cassette 10e is illustrated. While balance chamber 50 of FIGS. 19A and 19B is shown in connection with cassette 10e having rigid portion 140 and flexible portion 138, it is expressly contemplated to provide the balance chamber 50 of FIGS. 19A and 19B with a flexible sheeting cassette in which having a sole rigid portion 142. That is, rigid chamber 142 can be provided independently or separately and is not required to part of a larger rigid portion 140.

As illustrated, sheet 74a butts against a rigid backing member 146. Rigid backing member 146 can be provided with cassette 10d or is alternatively part of dialysis machine 100d operating with cassette 10d. Backing plate 146 constrains lower balance chamber compartment 54b to expand into the cavity formed by rigid chamber 142 when lower balance chamber compartment 54d is filled. Valve seats 28k and 28m are shown figuratively in cooperation with rigid chamber 142. Likewise, valve seats 28j and 28l are shown figuratively in cooperation with sheets 74a and 74b. For purposes of illustration, valve seats are shown with an "X" when in a closed fluid state and without an "X" when in an open or fluid flow state.

In FIG. 19A, the valve actuators operating with valve seats 28j and 28m cause the seats to be closed, while the valve actuators operating with valve seats 28k and 28l cause those seats to be open. In this valve state configuration, upper balance chamber compartment 54a fills with a volume of fluid 116, while lower balance chamber compartment 54b expels a like volume of fluid to a desired destination. In FIG. 19B, the valve actuators operating with valve seats 28k and 28l cause those seats to be closed, while the actuators operating with valve seats 28j and 28m cause those seats to be open. Here, lower balance chamber compartment 54b fills with fluid 116, while a like volume of fluid is dispensed from upper balance chamber compartment 54a, past valve seat 28m, to a desired destination.

The rigid chamber version of balance chamber 50 can be provided singly in a cassette, for example as shown in FIGS. 1 and 17 with cassettes 28a and 28d. Alternatively, two or more rigid chamber versions of balance chamber 50 are provided in a cassette, such as discussed in connection with cassette 10c of FIG. 3. Under normal matched flow circum-

stances, fresh fluid enters one of the compartments **54a** or **54b** dispensing spent fluid from the other compartment, and vice versa. Rigid chamber balance chamber **50** can alternatively be used for UF only, in which case spent fluid is delivered to both compartments **54a** and **54b**.

Referring now to FIGS. **20A** to **20D**, an alternative embodiment for balance chamber **50** employing the flexible sheet **74a** to **74c** is illustrated. Balance chamber **50** in FIGS. **20A** to **20D** incorporates tubes **156a** and **156b** as balance chamber inlet and tubes **158a** and **158b** as balance chamber outlets. Tubes **156a**, **156b**, **158a** and **158b** can be made of any suitable medical grade material, such as PVC, non-DEHP PVC, polybutadiene (“PB”), ethylene vinyl acetate (“EVA”), polypropylene (“PP”) blend, polyethylene (“PE”) blend, Kraton blend and polyolefin blends. The tubes are sealed in place along seals **72l**. Upper and lower seals **72e** and **72f** discussed above in connection with FIGS. **6** and **7** are made to form upper balance chamber compartment **54a** and lower balance chamber compartment **54b**. Inlet tube **156a** and outlet tube **158a** communicate fluidly with upper balance chamber compartment **54a**, while inlet tube **156b** and outlet tube **158b** communicate fluidly with lower balance chamber compartment **54b**.

Inner ends **160** of balance chamber inlet tubes **156a** and **156b** and balance chamber outlet tubes **158a** and **158b** are configured to be aligned with the circular chambers formed by seals **72e** and **72f**, so as to allow first and third sheets **74a** and **74c** to be pulled apart against respective inner walls of the balance chamber formerly members located inside the dialysis machine, such as chamber walls **102a** and **102b** shown in FIG. **7**. Middle sheet **74b** is sealed to the bottom of tubes **156a** and **158a** so that fluid entering from tube **156a** can flow only into upper compartment **54a**. Middle sheet **74b** is sealed around the top of inner ends **160** of tubes **156b** and **158b**, so that fluid entering sheet and tube type balance chamber **50** through **156b** can enter only into bottom compartment **54b** of balance chamber **50**. Otherwise, middle sheet **74b** is free to move back and forth within outer sheets **74a** and **74c** when balance chamber **50** is in operation.

FIGS. **20C** and **20D** illustrate that sheets **74a** to **74c** have semicircular bends **76**. Bends **76** can be preformed or at least partially preformed, e.g., via thermoforming. Alternatively, bends **76** are formed during the process of sealing sheets **74a** to **74c** about tubes **156** and **158**. Bends **76** are made outwardly in outer sheets **74a** and **74c**. Bends **76** in middle sheet **74b** alternate direction as needed. Depending on which side is being welded, seal **72l** may weld two sheets **74a/74b** or **74b/74c** or one sheet **74a** or **74b** to tubes **156a** or **156b**.

In the illustrated embodiment, sheet and tube type balance chamber **50** is provided as a separate apparatus that can be connected fluidly to another part of the disposable unit or the dialysis system. To that end, tubes **156a** to **158b** can be as long as needed to be connected to the other part of the dialysate circuit. In an alternative embodiment, two or more balance chambers **50** having the configuration of FIGS. **20A** to **20D** are formed via sheets **74a** to **74c** and two or more sets of tubes **156a** to **158b**. Further alternatively, one or more of the balance chambers **50** of FIGS. **20A** to **20D** is provided in a cassette such as cassettes **10a** to **10d**, which contain most if not all of the components of the dialysate circuit, notwithstanding the bags, patient connection and associated tubing.

Tubes **156a** to **158b** can have or include valve seats, such as valve seats **28j** to **28l** described above in connection with the balance chamber **50** of FIG. **1**. Alternatively, automated pinch or tubing clamps are used to clamp a portion of tubes **156a** to **158b** without needing a modified valve seat area. Balance

chamber **50** of FIGS. **20A** to **20D** can be used in any of the cassettes described herein employing one or more balance chamber.

Referring now to FIGS. **21A** to **21G**, an alternative flexible sheeting cassette **10e** is shown in operation with a hemodialysis machine **100e**, which in one preferred embodiment is a home hemodialysis (“HHD”) machine. Alternatively, cassette **10e** can be used with any of the dialysis therapies discussed herein. As discussed in the parent application, hemodialysis typically takes place in a clinic or center, in which the dialysate is made online using a water source and concentrates. In a home setting, a similar type of online dialysate generation unit is also used typically. These units are large and require the dialysis machine to be connected to a source of water. In the embodiment illustrated in FIGS. **21A** to **21G** and in the parent application, an alternative system is shown, which uses dialysate supplied from one or more supply bag, and which can provide convective clearance in addition to diffusive clearance. Alternatively, the blood disposable is combined with the dialysate disposable. In FIGS. **21B** and **21F**, a separate blood cassette **150** is provided.

FIGS. **21A** and **21C** to **21E** illustrate flexible sheeting cassette **10e**. Cassette **21e** differs from the above described cassettes in a number of ways. One difference is that separate peristaltic pumping tubes **148** and **154** are used instead of the flexible sheeting cassette pumping portion **30** shown and described above for example in connection with FIGS. **1**, **3** and **5**. A second difference is that the manifolding of the different supply and drain bags is done via tubing external to the flexible sheets **74a** to **74c** of cassette **10e**. In FIG. **21A**, the peristaltic pump actuators operating with dialysate line **148** and UF line **154** drive fluid to the inlets of balance chambers **50a** and **50b**. In an HHD therapy fluid exits the valved outlets of balance chambers **50a** and **50b** to either a dialyzer or the drain as described above. As before, balance chambers **50** operate as intermediate metering devices that meter a like volume of fluid to the drain and the dialyzer. Any of the methods for controlling ultrafiltration described above can be used with flexible sheeting cassette **10e**. For example, a number of strokes of balance chamber **50** can be dedicated UF strokes, in which spent fluid is pumped into both halves of balance chambers **50a** and **50b**. Alternatively, a separate UF balance chamber can be provided.

As seen in FIGS. **21A** and **21E**, fresh dialysate is pumped from one of the supply bags through a respective supply line **18a** to **18e**, into a manifold **162** and a dialysate pumping tube **148**, which operates with a peristaltic dialysate pump actuator. The peristaltic dialysate pump pumps fresh dialysate through inlet connector **16**, through integrated inline fluid heating pathway **42b**, and into one of the balance chambers **50a** or **50b**. Any air egressing from the heated solution is allowed to vent through vent **44**. In an embodiment, cassette **10e** is mounted vertically as shown in FIGS. **21A** and **21E**, such that air automatically rises to the top of cassette **10e** and is released through air vent **44** and vent line **164** (FIG. **21E**). This reduces the number valve actuators and seats as discussed above in connection with cassettes **10a** to **10c**. That is, any air is purged automatically without having to shutdown the normal operation of the machine.

The pumping of fresh dialysate into an inlet compartment of one of balance chambers **50a** and **50b** causes a like amount of spent fluid already residing in that balance chamber to be pumped via drainline **24** to drain. At the same time, the UF pump actuator operating with UF pump line **154** pumps spent fluid from the dialyzer, through from-patient line **152b**, into the inlet compartment of the other of balance chambers **50a**

and **50b**. Such action causes a like volume of fresh fluid to be pumped through patient connector **62a** and to-patient line **152a** to the dialyzer.

As seen in FIG. **21A**, a tubing organizer **168** is provided to hold supply lines **18a** to **18e**, drainline **24**, vent line **164**, to-dialyzer line **152a** and from-dialyzer line **152b** in an organized manner and enable cassette **10e** and associated tubes to be mounted readily. FIG. **21A** also shows darkened areas **188** cooperating with manifold **162**. Darkened areas **188** indicate portions of the associated tubes that are pinched closed to selectively allow fresh dialysate to be pulled from a desired supply bag **12** and spent dialysate to be pumped to drain bag **14** or one of the supply bags **12** being used as a drain bag.

Referring now to FIGS. **21C** and **21D**, a number of additional features of flexible sheeting cassette **10e** are illustrated. The schematic side view of FIG. **21D** illustrates that sheets **74a**, **74b** and **74c** are formed from a single sheet of material, which is folded twice to produce the three layers **74** (referring collectively to layers **24a** to **24c**). This allows the number of outer edge seams or seals to be reduced and also helps with the alignment of separate layers **74a** to **74c**. It should be appreciated that any of the flexible sheeting cassettes described herein can be formed using a single folded sheet, two sheets with one fold or three separate sheets, etc.

FIGS. **21C** and **21D** also show first weld areas **190a** in which only first sheet **74a** is welded to or otherwise fixed to sheet **74b**. Weld areas **190b** are also shown in which all three sheets **74a** to **74c** are welded or adhered together. FIG. **21C** also shows third areas **190c** in which only the second layer **74b** is welded to or otherwise fixed to third layer **74c**. This selective welding enables cassette **10e** to be made efficiently. Welding of three sheets does not have to be made in areas in which only two sheets need to be welded together. However, the three sheets can be welded or otherwise attached in areas in which it is required to do so. In general, two layer welds or glue joints **190a** and **190c** are required when flow in one layer is desired but not in another layer. In an alternative embodiment, three layer welds **190b** (except for periphery three layer welds and three layer welds for inlet and outlet ports) are eliminated and replaced with the compression seals described below in connection with FIGS. **24A**, **24B**, **25A**, **25B**, **26A**, **26B** and **28**.

In FIG. **21C**, selective welding occurs in areas associated with balance chambers **50a** and **50b**. FIG. **6** provides further information on how three sheeted balance chambers **50** can be welded together. Serpentine pathway **42b** is formed from a three sheet weld. This enables fluid heating pathway **42b** to extend spatially efficiently between sheets **74a** and **74b** and sheets **74b** and **74c**.

FIGS. **21C** and **21D** illustrate that the fluid travels between different layers or sheeting pairs using apertures **96** made in desired places in middle sheet **74b**. Fluid for example enters single supply connector **16** in a first pathway between sheets **74b** and **74c**. An aperture **96a** enables the fluid to travel into a portion of fluid heating pathway **42b** located between sheets **74a** and **74b**, in which it is heated a first time. Next, the fluid moves through an aperture **96b** into a second portion of fluid heating pathway **42b** located between sheets **74b** and **74c**. Any air egressing the heater solution is vented through the top of cassette **10e** via event **44**. Next, the heated fluid enters the balance chamber area, which uses all three sheets **74a** to **74c** in one embodiment. The fresh fluid leaves through a balance chamber compartment located between sheet **74b** and **74c** to the dialyzer through two patient connector **62a**. Spent fluid returns from the dialyzer to cassette **10e** via from patient connector **62b** into a balance chamber compartment located

between sheets **74a** and **74b**. The spent fluid is sent to drain via drain connector **22** located between sheets **74a** and **74b**.

Referring now to FIGS. **21B** and **21F**, one embodiment of a blood cassette **150** used with HD, HHD and HF is illustrated. Blood cassette **150** is also mounted vertically as illustrated in one embodiment. Cassette **150** includes a rigid portion **170** having a rigid housing **172** and a flexible membrane **174** made of any of the materials discussed above attached to housing **172**. Rigid portion **170** is made from a suitable material, such as polyvinyl chloride ("PVC"), acrylic, ABS, polycarbonate, polyolefin blends. Housing **172** includes or defines a from-patient port **176**, a to-patient port **178**, a saline port **180**, a vent **44**, a to-dialyzer port **182** and a from-dialyzer port **184**. As seen FIGS. **21B** and **21F** ports, such as ports **178** and **180**, port **184** and vent **44** can be formed in different relative locations along housing **172**.

FIG. **21B** illustrates valve seats **28x** to **28z** operating with the from-patient line, to-patient line and the saline line, respectively. A peristaltic pump actuator operates with blood pump line **166** to pump blood from the patient, to cassette **150** to the dialyzer, back to cassette **150** and then back to the patient. Fluid received from the dialyzer enters an air separation chamber **192** before being returned to the patient. Blood **186** collects at the bottom of air separation chamber, while any air in the blood raises to the top of air separation chamber **192**. Air separation chamber **192** can further include a vent **44**, such as a hydrophobic membrane, which allows air to be purged from cassette **150**.

The operation of blood cassette **150** of FIG. **21F** is similar to the operation described in connection with FIG. **21B**. Here, however, valve seat **28y** operates with to-dialyzer line connected to to-dialyzer port **182**. Valve seat **28x** controls the fluid entering cassette **150** from the patient as shown in FIG. **21B**. Valve seat **21z** controls the flow of saline into the cassette. Air separation chamber **192** operates as before, in which air at the top of chamber **192** can exit cassette **150** via vent **44**. Blood at the bottom of air separation chamber **192** flows to the patient through to-patient port **178**. FIG. **21F** further illustrates that a flexible sheet **174** is welded or adhered to rigid portion **172** of housing **170**. The flexible sheet **174** enables a valve actuator to press valve seats **28x** to **28z** to open/close a respective fluid flow path. As further illustrated in FIG. **21F**, blood cassette **150** includes or provides sensing areas **194a** and **194b** to sense a parameter of the blood, such as arterial pressure, venous pressure or blood temperature.

Cassette **150** illustrates components associated with a blood cassette used with HD, HHD, HF, HDF and any combination thereof as described in the parent application. As seen, the blood cassette can be provided as a separate cassette **150** installed separately from a dialysate cassette **10a** to **10b**. Alternatively, the components of the blood cassette are integrated with any one of dialysate cassettes **10** disclosed herein.

Referring now to FIG. **21G**, a top view of hemodialysis machine **100e** illustrates one embodiment for mounting cassette **10e**, the various supply bags **12** and drain bag **14**. Cassette **10e** can be placed on an angle relative to the top of machine **100e**, so as to create at least a slight vertical component to the mounting of cassette **10e** for venting purposes discussed above. Supply bags **12** and drain bag **14** are supported by the top of machine **100e** and are connected fluidly to cassette **10e** before or after the cassette is mounted to machine **100e**. Machine **100e** includes the user interface **196**, which enables the patient or caregiver to begin, control and monitor therapy. User interface **196** can use a touch screen overlay operable with a touch screen controller and/or membrane switches as desired.

Referring now to FIGS. 22A to 22D, a further alternative system **100f** employing an alternative flexible sheeting cassette **10f** is illustrated. System **100f** is well-suited to perform hemodialysis, such as home hemodialysis. Here, system **100f** also uses a second blood cassette, which can be similar to or the same as blood cassette **150** described above. FIG. 22A illustrates one embodiment for loading the cassettes **10f** and **150** into machine **100f**. Here, the dialysate components are located on one side of user interface **196**, while the blood components are located on the other side of user interface **196**. This configuration makes loading the cassettes relatively easy for the user and also allows the valve and pump actuators and heater located within machine **100e** to be mounted efficiently, reducing the overall size of machine **100f**.

In machine **100f**, cassette **10f** is positioned vertically, which is advantageous for air purging purposes described above. Machine **100f** includes two peristaltic pump actuators **90**, one of which drives fluid through a dialysate tube, while the other drives fluid through a UF tube, similar to the arrangement described above for cassette **10e**. A separate heater bag **40** described above in connection with FIG. 1 extends to the right from a rigid housing portion **200** of cassette **100f**. Rigid housing portion **200** as shown in more detail below defines flow paths and associated valve seats. Accordingly, the valve actuators of machine **100f** are located behind rigid cassette portion **200** of cassette **10f**. A plate heater or other type of heater is located behind heater bag **40**. A dual balance chamber flexible membrane component **198** of cassette **10f** resides beneath rigid portion **200**. As discussed herein, peristaltic pump actuators **90** drive fresh and spent fluid alternatively through the inlet compartments of balance chambers **50a** and **50b**. A hinged door **202** enables cassette **10f**, including its rigid portion **200**, balance chamber component **198** and heater bag **40** to be inserted and removed readily from machine **100f**.

Referring now to FIG. 22B, a more detailed view of cassette **10f** is illustrated. As discussed, cassette **10f** includes a rigid portion **200** connected fluidly to a separate heater bag **40** and a balance chamber unit **198**. Cassette **10f** therefore differs from cassette **10e** in that the heating and balance chamber functions are done via the flexible sheeting membranes, while valve actuation is performed using a rigid member **200** in combination with a flexible sheet **202**. Valve actuators, e.g., spring-loaded closed, pneumatically operated open actuators, operate with valve seats **28** to open and close selected flow paths as desired. Cassette **10f** also includes separate peristaltic pumping tubes **148** and **154** described above in connection with cassette **10e**. Heater bag **40** includes a serpentine heating pathway (not illustrated) and communicates with rigid member **200** via to- and from-heater lines **38a** and **38b**, respectively. Balance chamber unit **198** also communicates with rigid valve member **200** via port connectors and tubes as illustrated.

Balance chamber unit **198** is illustrated in more detail in FIGS. 22C and 22D. Balance chamber unit **198** is similar to the flexible sheeting balance chamber **50** described above in connection with FIGS. 20A to 20D. Here, unit **198** provides two balance chambers **50a** and **50b**, which are made of flexible sheets **74a** to **74c**, fresh fluid tubes **156** and spent fluid tubes **158**. As seen best in FIG. 22D, each compartment of balance chambers **50a** and **50b** communicates with only one of fresh tube **156** or spent **158**. Fresh tube **156** communicates with a first balance chamber compartment located between sheets **74a** and **74b**, while spent tube **158** communicates fluidly with a second balance chamber compartment located between sheets **74b** and **74c**. Balance chambers **50a** and **50b**

each include seals **72e**, **72f** and **72l** as described above in connection with FIGS. 20A to 20D.

FIG. 22D illustrates that sheets **74a** to **74c** have semicircular bends **76**, similar to that of balance chamber **50** of FIGS. 20A to 20D. Bends **76** can be preformed or at least partially preformed, e.g., via thermoforming. Alternatively, bends **76** are formed during the process of sealing sheets **74a** to **74c** about tubes **156** and **158**. Bends **76** are made outwardly in outer sheets **74a** and **74c**. Bends **76** in middle sheet **74b** alternate direction for each of balance chambers **50a** and **50b**. As seen, each tube **156** and **158** has a single sheet **74a** or **74c** welded on one side and two sheets **74a** or **74c** in combination with middle sheet **74b** welded on its other side. In one embodiment, tubes **156** and **158** are welded to middle sheet **74b** first. Outer sheets **74a** and **74c** are then welded to middle sheet **74b** and the exposed parts of tubes **156** and **158**.

In operation, fresh fluid enters and leaves through tube **156**. Spent fluid enters and leaves through tube **158**. That is, there is not a separate inlet and outlet tube for each balance chamber compartment is the case with balance chamber **50** of FIGS. 20A to 20D, which has two fresh tubes **156a** and **156b** and two spent tubes **158a** and **158b**. Rather, the same tube acts as the fresh or spent fluid inlet and fluid outlet for its compartment. Valves and flow paths are configured within rigid member **200** to direct the flow into or out of balance chambers **50a** and **50b** as desired.

Fresh fluid entering the fresh balance chamber compartment between sheets **74a** and **74b** through tube **156** causes middle sheet **74b** to dispel a like amount of spent fluid from spent compartment between sheets **74b** and **74c** through spent tube **158**. While this occurs in one of balance chambers **50a** and **50b**, spent fluid enters spent compartment between sheets **74b** and **74c** of the other balance chamber, flexing middle sheet **74b** to dispel a like amount of fresh fluid from fresh compartment between sheets **74a** and **74b** through fresh tube **156**. The sequence is then reversed. In this manner, an at least semicontinuous flow of fluid is sent to the patient or dialyzer and to drain.

Referring now to FIG. 23, a further alternative cassette is illustrated by cassette **10g**. Cassette **10g** is a simplified version of cassette **10e**. Cassette **10g** includes supply lines **18a** to **18e**, drainline **24**, dialysate pump tube **148**, return pump tube **154**, inline fluid heating pathway **42b**, vent **44**, vent line **164**, to-patient connector **62a**, to-dialyzer line **152a**, and from-dialyzer line **152b**. The primary difference between cassette **10g** and cassette **10e** is that balance chambers **50a** and **50b** used with cassette **10e** are not used with cassette **10g**. That is, volumetric control of fluid is not performed using matched flow equalizers or balance chambers **50a** and **50b** with flexible sheeting cassette **10g**. Instead, another method is used, such as via gravimetric or weight control of fluid delivered and removed from the patient or via a flow management system ("FMS") used with a HomeChoice® dialysis machine marketed by the assignee of the present application. The body of sheeting cassette **10g** can include valve seat and flow paths as needed to direct flow in a desired manner. Alternatively, flow can be controlled by clamping and unclamping the tubes connected to cassette **10g**, in which case cassette **10g** serves primarily as a fluid heating pathway. The flow paths, valve seats and fluid heating pathway **42b** can be provided via two sheets **74a** and **74b** or three sheets **74a** to **74c** as has described herein or can have a rigid component, such as rigid frame.

Referring now to FIGS. 24A and 24B, a further alternative system **100h** employing flexible membrane cassette **10h** is illustrated. System **100h** is well-suited to perform hemodialysis, such as home hemodialysis. System **100h** uses a blood

cassette, such as cassette **150**. FIG. **24A** shows system **100h** without cassette **10h** loaded. FIG. **24B** shows system **100h** with cassette **10h** loaded.

Cassette **10h** is simplified to a large extent because mating die plates **210a** and **210b** of machine **100h** clamp together around cassette **10h** to form the balance chamber portion, fluid heating pathways and other fluid flow paths of the cassette as installed. That is, the balance chamber portion, pathways, etc., do not have to be preformed in cassette **10h** prior to loading. The closing of door **202** against wall **220** of machine **100h** instead forms the fluid-tight passageways mechanically. Cassette **10h** is preformed as a pouch **212** as seen in FIG. **25B**, which is made of three sheets **74a** to **74c** or two sheets **74a** and **74b** as necessary to form the desired components. Pouch **212** is connected fluidly to to-dialyzer line **152a**, from-dialyzer line **152b**, vent line **164**, inlet connector **16**, supply lines **18a** to **18f** and drainline **24** as seen further in FIG. **24b**.

Die plate **210a** is formed hinged door **202**. Matching die plate **210b** is formed on wall **220** of machine or system **100h**. In the illustrated embodiment, die plate **210a** includes heating pathway forming ridges **214a** that mate with heating pathway forming ridges **214b** of die plate **210b**. Die plate **210a** includes balance chamber forming ridges **216a** that mate with balance chamber forming ridges **216b** of die plate **210b**. Die plates **210a** and **210b** also form or include tube/connector accepting grooves **218a** and **218b**, respectively, which secure tubes **152a**, **152b**, and **164** in place when door **202** is closed without crimping or closing the tubes. Die plates **210a** and **210b** alternatively or additionally form any other additional flexible sheeting apparatus discussed herein, such as volumetric pumping portions **70**, UF meter portions internal flow paths **26**, valve seats **28**, etc.

At least one of die plates **210a** and **210b** is integrated with component activation, such as, a heater, pump actuator, balance chamber actuator and/or valve actuator. Heating is accomplished via electrical resistance plate heating, inductive heating, radiant heating and/or ultrasonic heating. FIG. **25A** shows one embodiment of an in-line electrical resistance or plate heater configured to heat a fluid heating pathway formed by mechanical clamping. FIG. **25B** shows a separate heater having heating pathway forming clamshell sides, the teachings of which are also applicable to system **100h**. FIGS. **26A** and **26B** show a balance chamber portion of a flexible sheeting cassette formed via mechanical clamshell ridges, which can be activated pneumatically, mechanically, hydraulically or in the illustrated case electromagnetically. FIG. **28** shows a volumetric pump portion of a flexible sheeting cassette formed via mechanical clamshell ridges, which can also be activated pneumatically, mechanically, hydraulically or in the illustrated case electromagnetically. System **100h** can integrate any of these technologies into one or more of die plates **210a** and **210b**.

In the illustrated embodiment, pouch **212** is shown without any inner seams, except those needed to seal to connectors, e.g., connector **16**, and/or tubes **152a**, **152b** and **164**. It is contemplated to alternatively provide internal safety seams to mitigate damage due to leaking. For example, a seam could be provided to separate the fluid pathway portion of pouch **212** from the balance chamber portion of the pouch. Another seam could be provided to separate or isolate balance chamber portion **50a** from balance chamber portion **50b**, and so on. The safety seams can have any desired shape or pattern but can advantageously be simpler than the shape or pattern needed to form the flow component portions outright. Safety seams can be between sheets **74a** and **74b**, **74b** and **74c** and between all three sheets **74a** to **74c**.

It is alternatively expressly contemplated to form the two sheet seals, for instance, between sheets **74a** and **74b** or **74b** and **74c**, using the bonding or welding methods described above to form the actual flow components having two-sheet seals. Mechanical clamshell sealing here is used anywhere that a seal between all three sheets **74a** to **74c** is needed. Here again, the overall number and pattern of the welds or bonds should be lessened and simplified, respectively.

Referring now to FIG. **25A**, the heating portion of cassette **10h** formed by mechanical clamping heating pathway forming ridges **214a** and **214b** is illustrated. Cassette **10h** as shown in FIG. **25B** includes a pouch **212**, which receives fresh dialysate via fresh fluid inlet connector **16**. Ridges **214a** and **214b** form an inline fluid heating pathway **42b**, which receives the fresh fluid from inlet connector **16**. Inline fluid heating pathway **42b** serpentine back and forth as shown above to collect heat. Heated dialysate leaves through internal pathway **222**, which is also formed via mechanical clamping. Heated fluid through pathway **222** travels to balance chambers **50a** and **50b** or to a volumetric pump **70** for example.

In the illustrated embodiment clamping ridges **214a** and **214g** are also heating elements, for example, aluminum plate heating elements. Further elements **224a** and **224b** are connected to door **202** and machine wall **202**, which can also be electrical resistance elements. In one implementation, the heat actuator is a power supply that supplies power, e.g., 200 watts, to resistance elements **214a**, **214b**, **224a** and **224b**. Alternative types of heat actuators include inductive, radiant, connective, ultrasonic or a combination of heating types. Clamping ridges **214a** and **214b** can but do not have to be heat providing.

As illustrated, the heater using whatever type(s) of heat transfer is capable in one embodiment of heating dialysate starting from a temperature of about five to about thirty °C. to a temperature of about thirty-seven °C. or body temperature and at a flowrate of from zero to about three-hundred ml/min. A controller (not illustrated) within machine **100h** controls a duty cycle or power on/power off cycle in one embodiment to accommodate different starting dialysate temperatures and different dialysate flowrates. The controller can be a delegate or subordinate processor operating with a supervisory processor and a safety processor. An outflow fluid temperature monitor **226** senses the temperature of dialysate leaving fluid heating pathway **42b** and provides feedback to the controller to increase or decrease the duty cycle as needed to achieve the desired outflow temperature.

Referring now to FIG. **25B**, a separable fluid heater **240** employing mechanical clamping to create a fluid heating pathway (e.g., like pathway **42a** of FIGS. **1** and **3**) within the separate heater **240** is illustrated. Separate fluid heater **240** can be used for example in system **100a** of FIG. **1**, system **100c** of FIG. **3**, and cassette **10f** of FIGS. **22A** and **22B**. Heater **240** employs any of the types of heating in any combination discussed herein.

A fluid heating pouch **230** is connected to heater lines **38a** and **38b** through any method described herein. Materials for pouches **212**, **230** include any of those for sheets **74a** to **74c**. Materials for tubes **38a** and **38b** include any of those for the tubing described herein. As seen, heating pouch **230** as formed is simpler than fluid heating pathway **42a** of separate heater **40** of FIGS. **1** and **3**.

Heater **240** in the illustrated embodiment includes a clamshell configuration, in which first and second heating enclosures **242** and **244** are connected hinged together. When closed, heating path forming ridges **214a** and **214b** of enclosures **242** and **244**, respectively, mate and clamp pouch **230**. Enclosures **242** and **244** also form or include grooves **218a**

and **218b**, respectively, which except lines **38a** and **38b**, respectively, allowing enclosures **242** and **244** to fit flushly together without crimping those lines.

Ridges **214a** and **214b** may or may not themselves be heating elements as described above in connection with FIG. **25A**. Enclosures **242** and **244** in an embodiment each include a heating plate **246a** and **246b**, respectively. Heating plates **246a** and **246b** heat fluid within the crimped fluid heating pathway, for example, according to the temperatures and flowrates described above in connection with FIG. **25A**.

Referring now to FIGS. **26A** and **26B**, an alternative apparatus and method for operating a balance chamber **250** is illustrated. One primary difference illustrated by FIG. **26A** is that balance chamber **250** is driven magnetically and not via a separate pump as has been discussed previously. Middle sheet **74b** includes outer plies **74d** and **74e**, which sandwich a layer ferromagnetic material **252**, such as carbon or iron. Ferromagnetic material **252** is thin enough to allow middle sheet **74b** to flex back and forth as necessary within a chamber formed by chamber forming members **102a** and **102b**. Outer plies **74d** and **74e** can be of any material listed above for sheets **74a** to **74c**. Alternatively, ferromagnetic material **252** is impregnated or interspersed, e.g., as a powder or grain, into a single ply sheet **74b**. In any case, middle, moving sheet **252** needs to be compatible with sterile or near sterile medical fluids.

Balance chamber **250** is shown in operation with a portion of a dialysis machine **100** (e.g., **100a**, **100c**, **100e**, **100f** and **100h**) operating with a cassette **10** (e.g., cassette **10a**, **10c**, **10e**, **10f** and **10h**, respectively). Dialysis machine **100** includes or defines first and second chamber forming members **102a** and **102b**. For example, one of members of **102a** or **102b** is stationary and configured to accept flexible sheeting cassette **10** (e.g., formed in wall **220** of machine **100h**), while the other of chamber forming members **102a** or **102b** is part of a door (e.g., door **202**) that is closed onto the opposing side of flexible sheeting cassette **10** after it has been loaded into dialysis machine **100**.

Electromagnets **254a** and **254b** in the illustrated embodiment are embedded within members **102a** and **102b**, respectively, creating a magnetic field around the chamber, which can be modulated and polarized to pull ferromagnetic sheet **74b** to upper sheet **74a** or lower sheet **74c** of cassette **10**. Electromagnets **254a** and **254b** are alternatively coiled around spherical chamber-creating members **102a** and **102b**, respectively, and are in any case provided with enough mass to operate balance chamber **250** as discussed below.

Electromagnets **254a** and **254b** are each connected via leads **256** and **258** to a controller **248**. Controller **248** in one embodiment is a delegate or subordinate controller or printed circuit board ("PCB") that operates with a supervisory processor and a safety processor. Controller **248** in one embodiment also controls the valves operating with valve seats **28j** to **28m** (See FIGS. **1** and **3**), which switch in synchronization with the switching of electromagnets **254a** and **254b**.

To polarize electromagnet **254a**, controller **248** causes the leads **256** and **258** leading to electromagnet **254a** to power that electromagnet. To polarize electromagnet **254b**, controller **248** causes the leads **256** and **258** leading to electromagnet **254b** to power that electromagnet. When electromagnet **254a** is energized, ferromagnetic sheet **74b** is pulled to the top of balance chamber **250**. When electromagnet **254b** is energized, ferromagnetic sheet **74b** is pulled to the bottom of the chamber. In this manner, balance chamber **250** is self-powering or self-operating and provides a pumping function in addition to a metering function. A separate pump is not needed.

It is also contemplated that magnetically doped middle layer **74b** also allows for the measurement of position of the layer. By oscillating the power to electromagnetic coils **254a** and **254b**, it is possible to read the current generated by the inertial movement of the layer in the electromagnetic coil when the coil is off. This information relates to or is dependent on the velocity of the middle, magnetically doped layer **74b**. By integrating the velocity information it is possible to reliably determine position. This information can be used for determining flowrate out of or into the chamber and to determine when the chamber stroke has finished.

In the illustrated embodiment, chamber forming members **102a** and **102b** each define or include a port **104** to which a tube (not illustrated) is releasably or permanently secured via any of the methods and embodiments discussed herein. In an embodiment, after cassette **10** is loaded into machine **100**, a static negative pressure or vacuum is drawn on ports **104**, pulling first and third plies or sheets **74a** and **74c** against the inner at least substantially spherically shaped cavities defined by first and second members **102a** and **102b**. Flexible sheets **74a** to **74c** are made of a suitably stretchable, compliant, non-magnetic and leak-free material.

Although members **102a** and **102b** are shown defining at least substantially spherical shapes, other suitable cross-sectional shapes may be used, such as substantially triangular or substantially trapezoidal shapes. Further, although not illustrated, members **102a** and **102b** can define air channels that extend radially from ports **104** in various directions to help spread the vacuum across a larger surface of plies **74a** and **74c**. Once sheets **74a** and **74c** are pulled via vacuum against the inner surface of chamber forming members **102a** and **102b**, respectively, balance chamber **50** is ready for operation.

In one alternative embodiment, sheets **74a** and **74c** are rigid or semi-rigid and preformed having the, e.g., semicircular, chamber shape, making ports **104** and associated negative pressure unnecessary. In another alternative embodiment, electromagnets **254a** and **254b** and ferromagnetic sheet **74b** are employed with a balance chamber that is re-used, i.e., is not disposable, so that outer sheets **74a** and **74c** are not needed. That is, magnetic actuation can be used with any type of balance chamber and is expressly not limited to a cassette-based or flexible sheeting cassette-based application as shown here.

FIG. **26A** illustrates a state of operation in which no fluid has been delivered to balance chamber **250**. In the illustrated embodiment, valve seat **28l** is shown operating with a valve actuator **106**, which is part of machine **100**. Here, positive air pressure is applied to the port of actuator **106** to force a plunger **108** to compress valve seat **28l** against second sheet **74b**, closing balance chamber outlet **58a**. Actuator **106** includes an o-ring seal **110**, which creates a sliding seal between plunger **108** in the inner, e.g., cylindrical housing of valve actuator **106**. To open balance chamber outlet **58a**, a negative pressure is applied to port **106**, pulling plunger **108** upwards against stop **112**, enabling fluid to open seat **28l** and flow outwardly from upper balance chamber compartment **54a** through balance chamber outlet **58a**.

In operation, to fill upper balance chamber compartment **54a**, plunger **108** is pressurized, closing valve seat **28l** and balance chamber outlet **58a**. A similar valve actuator and plunger closes balance chamber inlet **56a**. Electromagnet **254a** is energized, pulling sheet **74b** against upper sheet **74a**. Next, the valve actuator and plunger operating with balance chamber inlet **56a** is opened, electromagnet **254a** is de-energized, electromagnet **254b** is energized, pulling sheet **74b**

fully across the chamber and against lower sheet **74c**, creating a vacuum and filling upper balance chamber compartment **54a**.

To empty upper balance chamber compartment **54a** and fill lower balance chamber compartment **54b**, the valve actuator and plunger operating with balance chamber inlet **56a** is closed, plunger **108** is pulled against stop **112**, opening valve seat **28l** and balance chamber outlet **58a**, electromagnet **254b** is de-energized, electromagnet **254a** is energized, pulling sheet **74b** fully across the chamber and against upper sheet **74a**, dispelling fluid from balance chamber compartment **54a**, through balance chamber outlet **58a** and simultaneously creating a vacuum within balance chamber compartment **54b**, filling such chamber. The cycle is then reversed using second balance chamber inlet **56b** and second balance chamber outlet **58b** (See FIG. 1) to dispel fluid from balance chamber compartment **54b** and simultaneously fill balance chamber compartment **54a**.

Because the volume defined by compartments **54a** and **54b** is fixed and because second sheet **74b** is pushed all the way against upper and lower sheets **74a** or **74c** in each half stroke, the same volume of fluid is outputted through balance chamber outlets **58a** and **58b** in each half stroke. In this manner fresh and spent fluid balancing and UF removal can be readily and accurately controlled.

It is also contemplated to impregnate plungers **108** with a ferromagnetic material and open and close valve seats **28** electromagnetically.

Referring now to FIG. 26B, FIG. 26A is rotated ninety degrees about an access through ports **104** to show one embodiment for creating balance chamber seals via mechanical clamping crimping. Chamber forming members **102a** and **102b** each define or include a balance chamber crimping ridge or ring **216a** and **216b** (described above in connection with FIGS. 24A and 24B). Rings **216a** and **216b** in an embodiment extend around the circumference of balance chamber **50** or **250**, except to allow for inlet and out let paths **56** and **58**. Rings **216a** and **216b** crimp together to seal sheets **74a** to **74c** mechanically enough to withstand the positive and negative pressures and variations of same within the chamber. Clamping rings **216a** and **216b** operate with any type of balance chamber operation, e.g., via separate pump or electromagnetic operation.

An outer safety ring seal **72m** may be provided optionally. Seal **72m** is formed via any of the techniques discussed herein. It serves to mitigate the damage from any dialysate escaping the mechanical seal formed by mechanical rings **216a** and **216b**. It also allows for tolerance in aligning cassette **10** within machine **100**.

Referring now to FIG. 27, one embodiment of a magnetically driven balance tube **260** is illustrated. A balance tube is discussed in connection with FIG. 45 of the parent application. As discussed in the parent application, balance tube **260** here includes a separator **262**, which functions similar to flexible membrane **74b** of balance chamber **250**. In the illustrated embodiment, separator **262** is a ball or spherical object that moves snugly within a cylindrical housing **264**. A pair of caps **266** and **268** are provided on either end of cylindrical housing **264**. Caps **266** and **268** seal to cylindrical tubing **264** via outer O-rings **270**. Separator or ball **262** seals to caps **266** and **268** via inner O-rings **272**. In an alternative embodiment, caps **266** and **268** are permanently or hermetically sealed to cylindrical tube **264**. Ports **274** and **276** are formed integrally with or are attached to caps **266** and **268**, respectively. Ports **274** and **276** seal to mating tubes via any mechanism known to those with skill in the art.

Separator **262** is impregnated with a ferromagnetic material, such as carbon or iron. For example, a carbon core could be covered with a shell made of a medically safe material. Electromagnets **254a** and **254b** are in one embodiment embedded within caps **266** and **268**, respectively, creating a magnetic field around separator **262**, which can be modulated and polarized to pull ferromagnetic separator **262** to upper cap **266** or lower cap **268**. Electromagnets **254a** and **254b** are each connected via leads **256** and **258** to a controller **248** described above. Electromagnets **254a** and **254b** are alternatively located outside of caps **266** and **268** and coiled instead around caps **266** and **268** and potentially end positions of tube **264**. Here, the magnets can be housed within the machine as opposed to being located with in tube **260**.

To polarize electromagnet **254a**, controller **248** causes the leads **256** and **258** leading to electromagnet **254a** to power that electromagnet. To polarize electromagnet **254b**, controller **248** causes the leads **256** and **258** leading to electromagnet **254b** to power that electromagnet. When electromagnet **254a** is energized, ferromagnetic separator **262** is pulled to cap **266**. When electromagnet **254b** is energized, ferromagnetic separator **262** is pulled to cap **268**. The movement of ball **262** pushes out and pulls in fresh/spent or spent/fresh fluid through port **274** or **276** upon each stroke. In this manner, balance tube **260** is self-powering or self-operating and provides a pumping function in addition to a metering function. A separate pump is not needed. As discussed above, magnetically impregnated separator **262** allows for its position to be determined within housing **264**.

In an embodiment, cylindrical tube **264** is translucent or transparent, so that an optical sensor can detect if ferromagnetic ball or separator **262** has properly reached the end of travel. Ultrasonic or other types of sensors may be used alternatively. Ferromagnetic ball or separator **262** is sized to fit snugly but smoothly within the interior of cylinder **264**. A small amount of mixing between fresh and effluent fluid may occur without substantially affecting the performance of the system. In an alternative embodiment, a cylindrical piston type separator is provided. In either case, ferromagnetic separator **262** may have additional sealing apparatus, such as wipers or deformable flanges that help to enhance the sliding or rolling seal as the case may be.

Balance tube **260** may be made of plastic or other suitable material. In an embodiment, balance tube **260** is a disposable item, which may be formed integrally with cassette **10** or attached to the cassette via tubing. O-rings and fittings may not be necessary if injection molded caps or assemblies are used. In addition, sensors such as ultrasonic or optical sensors, for the positioning of the separator can eliminate the need for sealing at the end of the tube.

Referring now to FIG. 28 an electromagnetically controlled volumetric pump **280** is illustrated. Volumetric pump **280** is shown operating with a dialysis machine **100**, such as machine **100b** (FIG. 2), which uses a cassette **10**, such as cassette **10b** (FIG. 2). Pump **280** can operate out of phase with a second electromagnetically controlled volumetric pump **280** in a manner discussed herein.

Machine **100** includes first and second pump chamber forming members **114a** and **114b**, which define the shape of the volumetric pump **280**. Cassette **10** is configured to be loaded within the machine **100** such that a circular flexible membrane portion of cassette **10** is in alignment with the spherically shaped chamber defined by pump chamber forming members **114a** and **114b**. Although the spherical shape shown in FIG. 28 is one suitable shape, other shapes could be defined for volumetric pump **280**, such as a trapezoidal or triangular shape. Also, valve seats **28q** and **28s** are aligned

with valve actuators **106** as shown. Valve actuators **106** operate as described above in connection with FIG. 7 and include a plunger **108**, which slides back and forth within the actuator body.

Pump **280** uses first and second flexible sheets **74a** and **74b**. Sheets **74a** and **74b** are each impregnated with a ferromagnetic material **252**, such as an inner carbon or iron layer. Electromagnets **254a** and **254b** are embedded within pump chamber forming members **114a** and **114b**, respectively, creating a magnetic field around sheets **74a** and **74b**, which can both be energized to pull ferromagnetic sheets **74a** and **74b** apart to upper and lower members **114a** and **114b**, respectively. Alternatively, only one of electromagnets **254a** and **254b** is energized, pulling both sheets **74a** and **74b** towards that electromagnet. Electromagnets **254a** and **254b** are each connected via leads **256** and **258** to a controller **248** as described above. They can alternatively be located outside of an winding around members **114a** and **114b**.

In an initial state (shown in FIG. 28), electromagnet **254b** is powered, which pulls first and second flexible sheets **74a** and **74b** to conform with the inner surface of lower chamber forming member **114b**. Initially, a positive pressure is applied to both valve actuators **106**, closing valve seats **28q** and **28s**. Again, valve actuators **106** can be any combination of pneumatically, mechanically, electrically and/or electromagnetically operated. As seen in FIG. 28, dialysate or medical fluid (including blood) **116** is pressurized against valve seat **28q**, but is precluded from entering into the sealed chamber of volumetric pump **280**.

In a second state, electromagnet **254b** continues to be powered as is the positive pressure applied to valve actuator **106** at valve seat **28s**. A negative pressure is applied to valve actuator **106** at valve seat **28q**, which pulls and holds plunger **108** to and against stop **112**, allowing fluid **116** to flow through pump inlet pathway **66b** and into the chamber of volumetric pump **280**. The force of fluid **116**, e.g., via gravity may be enough to cause first flexible member **74a** to be pushed against inner surface of upper pump chamber forming member **114a**. Alternatively or additionally, electromagnet **254a** is powered to pull first flexible sheet **74a** against the inner surface of upper member **114a**. This action causes a vacuum, which pulls fluid **116** into the pump chamber.

In a third state, valve seat **28q** is closed, while valve seat **28s** is opened. Power at electromagnet **254b** is maintained, so that sheet **74b** continues to be pulled against member **114b**. Power is removed from electromagnet **254a** causing electromagnet **254b** to pull upper flexible sheet **74a** against lower flexible sheet **74b** at member **114b**, which in turn causes fluid **116** to be pushed out of the at least substantially spherical chamber of volumetric pump **280**, through pump outlet pathway **68b**, to its desired destination. First and second membranes **74a** and **74b** are now at the initial state shown in FIG. 28, so that pump **280** is able to repeat the above described cycle as soon as valve seat **28s** is closed.

Because the volume formed by the chamber of members **114a** and **114b** is known and because the flexible sheets are moved repeatedly to the upper and lower surfaces of the chambers, the volume of fluid pumped with each stroke is known and repeatable. Accordingly, a separate volumetric control apparatus, such as balance chamber **50** or **250**, is not needed. The total volume of fluid pumped is equal to the volume of each stroke multiplied by the number of strokes. UF is controlled via one of the methods discussed above. As discussed above, magnetically impregnated sheet **74a** and **74b** allow for their position to be determined within chamber forming members **114a** and **114b**.

Many embodiments have been described herein for different flexible sheeting cassettes having varying degrees and types of fluid flow components and functionality. The parent application for this application referenced herein includes many different embodiments for hemodialysis hemofiltration and hemodiafiltration systems. In particular, many embodiments are shown using dual dialyzers and a flow restriction between the dialyzers, which causes both diffusive and convective clearances associated with HHD. The flexible sheeting cassettes described herein may be used for each of the systems described in the parent application, including but not limited to: (i) the volumetric pump-based HCHDF systems of FIGS. 1, 4 and 5, which provide diffusive and convective clearance; (ii) the volumetric pump-based HF systems of FIGS. 6 and 7; (iii) the alternative volumetric pump-based HDF system of FIG. 8; (iv) the volumetric pump-based regeneration systems of FIGS. 9 to 11; (v) the peristaltic pump-based HDF and HF systems of FIGS. 12 and 13; (vi) the co-current flow system of FIG. 14; the pneumatically controlled system of FIGS. 15 and 16; (vii) the single balance chamber systems of FIGS. 17 to 22; (viii) the torturous path system of FIGS. 24 and 29, wherein the tortuous paths are formed between the sheets or plies **74a** to **74u** in any of the manners described above; (ix) the dual balance chamber systems of FIGS. 25 and 26; (x) the weight measurement system of FIGS. 30 and 31; the enhanced convection of HDF filter of FIG. 32; (xi) the linear tubing pump systems of FIGS. 38 to 41; and (xii) the fluid heater of FIGS. 42 and 43.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present subject matter and without diminishing its intended advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

The invention claimed is:

1. A hemodialysis system comprising:

a dialyzer;

a blood pump;

a blood cassette operatively connected to the dialyzer and the blood pump;

a dialysate heater;

first and second peristaltic dialysate pumps; and

a dialysate cassette separate from the blood cassette, the dialysate cassette including an organizer configured to support a drain tube, a to-dialyzer tube and a from-dialyzer tube, the cassette further including a first pumping tube, a second pumping tube and an inline fluid heating pathway, the cassette when mounted for operation orienting (i) the first pumping tube for operation with the first peristaltic dialysate pump, (ii) the second pumping tube for operation with the second peristaltic dialysate pump and (iii) the fluid heating pathway for operation with the dialysate heater.

2. The hemodialysis system of claim 1, wherein the organizer is a rigid structure.

3. The hemodialysis system of claim 1, wherein the inline fluid heating pathway includes a bent tubular pathway.

4. The hemodialysis system of claim 1, wherein the inline fluid heating pathway includes a serpentine tubular pathway.

5. The hemodialysis system of claim 1, wherein the dialysate cassette includes a plurality of supply tubes supported by the organizer.

6. The hemodialysis system of claim 5, wherein the supply tubes and the drain tube are arranged in a row along the organizer.

45

7. The hemodialysis system of claim 5, wherein the supply tubes are each in fluid communication with a supply of dialysate.

8. The hemodialysis system of claim 1, wherein the first pumping tube is a to-dialyzer pumping tube, and wherein the fluid heating pathway is located between the to-dialyzer pumping tube and the to-dialyzer tube.

9. The hemodialysis system of claim 1, wherein the dialysate cassette includes rigid internal structures for orienting the first and second pumping tubes and the inline fluid heating pathway.

10. The hemodialysis system of claim 1, wherein the dialysate cassette includes at least one balance chamber for balancing dialysate traveling to and from the dialyzer.

11. The hemodialysis system of claim 1, wherein the dialysate cassette includes an air vent.

12. The hemodialysis system of claim 1, wherein the dialysate cassette is substantially planar such that the cassette can be mounted horizontally or vertically.

13. The hemodialysis system of claim 1, wherein the to-dialyzer tube and the from-dialyzer tube are disposed substantially parallel to one another.

14. The hemodialysis system of claim 1, wherein the drain tube is in fluid communication with a container that is initially a supply container.

15. The hemodialysis system of claim 14, which includes a valve, the dialysate cassette including an area operable with the valve to selectively allow (i) a supply of dialysate to be delivered from the container to the cassette or (ii) the container to receive spent dialysate from the drain tube.

16. A hemodialysis system comprising:

a dialyzer;

a blood pump;

a blood cassette operatively connected to the dialyzer and the blood pump;

a dialysate heater;

first and second peristaltic dialysate pumps; and

a dialysate cassette separate from the blood cassette, the dialysate cassette including an organizer configured to support a drain tube, a to-dialyzer tube and a from-dialyzer tube, the organizer further including internal

46

connectors for supporting and orienting a first pumping tube, a second pumping tube and an inline fluid heating pathway, the internal connectors when mounted for operation orienting (i) the first pumping tube for operation with the first peristaltic dialysate pump, (ii) the second pumping tube for operation with the second peristaltic dialysate pump and (iii) the fluid heating pathway for operation with the dialysate heater.

17. The hemodialysis system of claim 16, wherein the organizer further orients at least one of (i) the to-dialyzer tube towards the dialyzer, (ii) the from-dialyzer tube towards the dialyzer and (iii) the drain tube towards a drain.

18. The hemodialysis system of claim 16, wherein the drain tube is in communication with a container that is initially a dialysate supply container.

19. A hemodialysis system comprising:

a dialyzer;

a blood pump;

a blood cassette operatively connected to the dialyzer and the blood pump;

a dialysate heater;

a dialysate source;

first and second peristaltic dialysate pumps; and

a dialysate cassette separate from the blood cassette, the dialysate cassette including an organizer configured to support a drain tube, a to-dialyzer tube and a from-dialyzer tube, the organizer further including internal connectors for supporting and orienting a first pumping tube, a second pumping tube and an inline fluid heating pathway, the organizer when mounted for operation orienting (i) the to-dialyzer tube towards the dialyzer, (ii) the from-dialyzer tube towards the dialyzer and (iii) the drain tube towards the dialysate source.

20. The hemodialysis system of claim 19, wherein the organizer when mounted for operation further orients (i) the first pumping tube for operation with the first peristaltic dialysate pump, (ii) the second pumping tube for operation with the second peristaltic dialysate pump and (iii) the fluid heating pathway for operation with the dialysate heater.

* * * * *